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DOCTORAL DISSERTATION

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Abstract

Musculoskeletal disorders (MSDs) are a major cause of disability worldwide, and two conditions that are major contributors to the overall burden of MSDs are fractures and osteoarthritis (OA). The Swedish Health and Medical Services Act (HSL 2017:30) states that the goal of all health care services is good health and health care on equal terms for the entire population. However, there exists a well-known association between SES and health, where people with lower SES, generally, tend to have poorer health and higher mortality. This association is seen for a wide range of diseases, including MSDs. However, the knowledge about inequalities in MSDs in the Swedish health care system is limited. Thus, the aim of this thesis was to determine the association between SES and outcomes in MSDs, with focus on fractures and osteoarthritis, in order to identify potential health inequalities.

The studies in this thesis are based on individual-level register data from people resident in the Skåne region (study I and II) and the whole country of Sweden (study III and IV). Study I-III are open cohort studies, while study IV has a repeated cross-sectional design. In addition, study I and III have a multiple cause of death approach and co-twin control design, respectively. Educational attainment was used as an indicator for SES in all studies. Following data sources were used: Statistics Sweden, The National Board of Health and Welfare, The Skåne Healthcare Register, The Swedish Twin Registry (STR), and The Swedish Military Conscription Registry.

In study I, absolute and relative educational inequalities in non-hip and hip fracture-related mortality were examined using the slope index of inequality (SII) and relative index of inequality (RII), respectively. The study period was between 1998-2014, and 999,148 people were included. Generally, the absolute as well as the relative inequalities revealed higher fracture-related mortality in people with low vs. high education, suggesting that preventative and therapeutic interventions of fractures in low educated people should be targeted.

Study II assessed the association between education and all-cause and cause-specific mortality among patients with OA (123,993 people) in comparison to an OA-free reference cohort (121,318 people). The study period was from 1998 to 2014, and the inequalities were examined with SII and RII. The results showed that people with lower education, with or without OA, have higher all-cause and cause-specific mortality and that the inequalities observed in OA patients reflect the health inequalities in the population at large. In addition, the results suggest that OA patients, especially with lower education, have a greater burden of cardiovascular diseases, which implies that it is important to focus on the prevention and treatment of cardiovascular diseases in this group.

The aim of study III was to examine the association between educational attainment and knee and hip OA surgery using twin data. In total, 67,071 twins from the STR were included and the studied time period was between 1987-2016. The main analysis was Weibull within-between shared frailty model. When adjusting for genetics and early-life environment, there was no association between educational attainment and knee and hip OA surgery. However, a confounding familial effect in the association between educational attainment and knee OA surgery was found.

In study IV changes in prevalence and socioeconomic inequalities in knee and hip OA surgery and non-surgery specialist care visits were examined. The studied time period was 2001-2011, and the prevalence and inequalities were estimated for each year. The concentration Index was used to assess relative and absolute inequalities. The Blinder-Oaxaca decomposition method was used to examine the factors contributing to the changes between the years 2001 (4 794,693 people) and 2011 (5 359,186 people). The prevalence of all outcomes rose. Changes in the strength of the association between sociodemographic factors and OA outcomes contributed the most to the increase in knee OA outcomes. For hip OA outcomes, the increase was primarily due to changes in the characteristics of the populations over time. All outcomes were more concentrated among people with lower education. Absolute educational inequalities were either decreasing or steady over time, while there was a declining tendency in relative inequalities for all outcomes.

The overall conclusion of the thesis is that there are socioeconomic inequalities in fracture-related mortality and OA-related outcomes in favour of people with higher SES. The associations need to be investigated in more detail in order to be able to reduce the observed differences.

Key words: Education, Health Inequities, Fracture, Mortality, Osteoarthritis, Osteoarthritis Surgery, Sweden

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MADE IN SWEDEN

In dedication to my mother and father

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Preface

I have always been fascinated by natural science and human behaviour, and this was the reason why I started to study medicine. I started my medical studies at Lund University in 2012. My interest in the relationship between society and health was awakened during my studies, and in 2017 I conducted my master's thesis at the Clinical Epidemiology Unit at Lund University. Epidemiology and health inequality research immediately caught my interest. This, combined with the experience of being a part of a great research group, motivated me to start my doctoral studies at the same research unit in the same year. Since I started my doctoral studies, I have been a part-time PhD student, except for the months I have had full-time research as part of my medical internship and so-called *doktorandmånader* (three months of full-time research funded by the faculty). What concerns my clinical career, I graduated from the medical program in 2018, and between the years 2018-2020 I did my medical internship at the Lund University Hospital. Since 2021 I have been a resident in general medicine.

Health inequality is a problem that affects both the individual and society at large. To reduce inequalities, it is first necessary to identify potential health inequalities and the underlying mechanisms behind them. This thesis provides new insights into socioeconomic inequalities in musculoskeletal disorders, which in turn are a major cause of morbidity worldwide. I hope this thesis can be used as a starting point for further research.

I have greatly enjoyed doing this PhD, and through the studies I have gained knowledge and experiences that I am grateful for. I hope to continue combining research and clinical work in the future.

Abstract

Musculoskeletal disorders (MSDs) are a major cause of disability worldwide, and two conditions that are major contributors to the overall burden of MSDs are fractures and osteoarthritis (OA). The Swedish Health and Medical Services Act (HSL 2017:30) states that the goal of all health care services is good health and health care on equal terms for the entire population. However, there exists a well-known association between SES and health, where people with lower SES, generally, tend to have poorer health and higher mortality. This association is seen for a wide range of diseases, including MSDs. However, the knowledge about inequalities in MSDs in the Swedish health care system is limited. Thus, the aim of this thesis was to determine the association between SES and outcomes in MSDs, with focus on fractures and osteoarthritis, in order to identify potential health inequalities.

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The overall conclusion of the thesis is that there are socioeconomic inequalities in fracture-related mortality and OA-related outcomes in favour of people with higher SES. The associations need to be investigated in more detail in order to be able to reduce the observed differences.

List of papers

This thesis is based on the following studies, which have been reprinted with permission from the publishers. Throughout the thesis, the four studies are referred to with Roman numerals.

I. Lindéus M, Englund M, Kiadaliri A. Educational inequalities in fracture-related mortality using multiple cause of death data in the Skåne region, Sweden. *The Scandinavian Journal of Public Health*. 2020;48(1):72-79.

II. Lindéus M, Turkiewicz A, Englund M, Kiadaliri A. Socioeconomic inequalities in all-cause and cause-specific mortality among patients with osteoarthritis in the Skåne region of Sweden. *Arthritis Care & Research*. 2022;74(10):1704-1712.

III. Lindéus M, Turkiewicz A, Magnusson K, Englund M, Kiadaliri A. Does lower educational attainment increase the risk of osteoarthritis surgery? A Swedish twin study. *BMC Musculoskeletal Disorders*. 2023;24(1):72.

IV. Lindéus M, Peat G, Englund M, Kiadaliri A. Changes in educational inequalities in knee and hip OA surgery and non-surgery specialist care visits over time in Sweden. In manuscript.

Abbreviations

ASMR	Age-standardised mortality rates
BMI	Body mass index
BOA	Better management of patients with osteoarthritis
CI	Confidence interval
HR	Hazard ratio
ICD	International Classification of Diseases
LISA	The Longitudinal Integration Database of Health Insurance and Labour Market Studies
OA	Osteoarthritis
RIF	Recentered influence function
RII	Relative index of inequality
RR	Rate ratio
SES	Socioeconomic status
SHR	The Skåne Healthcare Register
SII	Slope index of inequality
STR	The Swedish Twin Registry
UCD	Underlying cause of death
WI	Wagstaff Index
YLDs	Years lived with disability

Introduction

The Swedish Health and Medical Services Act (HSL 2017:30) states that the goal of all health care services is good health and health care on equal terms for the entire population. Still, well-known health inequalities exist in Sweden, where people with lower socioeconomic status (SES), generally, tend to have poorer health status and higher mortality (1). This phenomenon is known as *the social gradient in health* and is seen globally regarding mortality as well as for a wide range of diseases (2), including musculoskeletal disorders.

Socioeconomic status and health

A person's health is a product of biological, environmental, and social factors, and this is illustrated in Figure 1. A well-known determinant of health is SES (3, 4). According to Oxford Reference SES is "*a descriptive term for the position of persons in society, based on a combination of occupational, economic, and educational criteria, usually expressed in ordered categories, that is, on an ordinal scale*"(5).

Health differences between individuals or groups are referred to as health inequality (3, 4). The term *health inequality* does not take into account whether the observed difference is just/unjust. In contrast, the term *health inequity* refers to a systematic difference in health that is unjust since it could have been preventable (3, 4). Thus, it has been suggested that one could consider health differences related to biological variations and free informed choice as just inequalities or unavoidable, while differences related to less choice in lifestyle, differences in working conditions and access to health care etc. are considered to be unjust and avoidable (4). In this thesis the term *health inequality* will be used.

Measurements of socioeconomic status

Different indicators of socioeconomic position can be used in health research, for instance: educational attainment, income, wealth, occupation, employment and housing etc. (3). A widely accepted indicator for SES in health inequality research is educational attainment (6). In this thesis educational attainment was used as an indicator for SES. Educational attainment is easy to measure and is less likely to fluctuate in comparison to income and occupation. Additionally, higher educational attainment offers, in general, better employment prospects and there is a strong association between educational attainment and income (7).

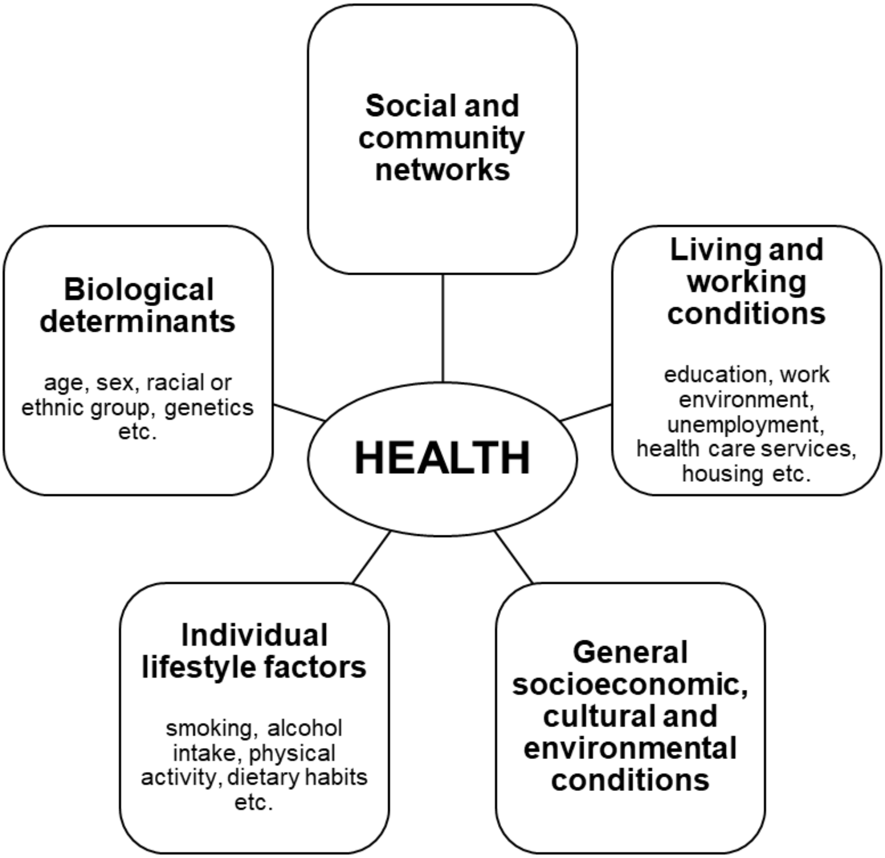


Figure 1. Determinants of health. The image is based on the Dahlgren-Whitehead model of health determinants (8).

Education in Sweden

In Sweden, compulsory schooling was introduced in 1842, and in the 1930s it was decided that the compulsory school should be at least seven years. The first version of the current compulsory school, with nine-years compulsory schooling, was introduced in the 1960s (9). What concerns secondary school, the first version of the current *Gymnasieskola* was introduced in the 1970s and replaced the previous school forms: *gymnasium*, *fackskola,* and *yrkesskola* (10). Post-secondary education is given at universities and university colleges (Swedish: *högskola*). The compulsory and secondary school is tuition-free (11). What concerns post-secondary education, Swedish citizens, along with citizens of the European

Union/European Economic Area, do not pay tuition at Swedish universities/university colleges. In addition, financial aid to students is available from the government (12).

Since the past few decades, the level of education of the Swedish population has increased substantially. As an example, in 2007 34% of people aged 20-64 years had some kind of post-secondary education (>12 years of education), while the corresponding percent in 1990 was 21%. It is estimated that the percentage of people with <9 years of education will drop from 31% in 1990 to 10% in 2030 (13). It is mainly among females where the level of education has increased (13). A report by Statistics Sweden from 2014 showed that level of education differs between age groups and the sexes (14). The study reported that it is most common to have <9 years of education in the oldest age group (55-64 years old) in the working population (14). Furthermore, in the working population men had, in all age groups in comparison to females, to a greater extent <9 years of education (14). In addition, for people aged 75 years and older, only 7-11% had a post-secondary education that was at least 16 years or more, and more men than females were in this group (14).

When comparing educational attainment of foreign-born people, which is a group that, generally, tend to have poorer health compared to Swedish-born (1), some educational differences were reported, where the former group has somewhat lower education (15). This difference concerns mainly low education, where there is a larger proportion foreign-born people (20%) with low education (primary education at most) compared to Sweden-born people (9%) (15). However, the proportion of people with post-secondary education is approximately the same among Sweden- and foreign-born people. What concerns highly educated people with at least three years of post-secondary education, the proportion is also equally large between the groups (15).

Why do health inequalities occur?

There exist different explanations on why health inequalities occur, such as *the health selection hypothesis, the indirect selection hypothesis*, explanations that point to differences in *material* and *psychosocial* factors, *behavioural* differences, and differences in *biomedical* factors (3).

The health selection hypothesis refers to the theory that health influences SES rather than the reverse. Thus, the theory implies that health inequalities emerge as a result of healthier people moving towards higher socioeconomic positions relative to less healthy people (3). In contrast, *the indirect selection hypothesis*, does not assume a causal association between SES and health. Instead, the theory suggests that there exist unknown factors (such as genetics, family background etc.) that influence both health and SES (16).

Socioeconomic differences in material resources and their effect on physical threats (like inadequate diet, poor housing, environmental exposures, physical hazards at work etc.) is another explanation of socioeconomic health inequalities (3, 17). As an example, income has been reported to be strongly associated with mortality (18).

Psychosocial factors as an explanation for health disparities posits that people with lower SES might experience more negative psychological stress (due to feelings from social exclusion, stress, discrimination, low social support etc.) which in turn affects their health in a negative way. The mechanism is thought to be an activation of the biological stress response which in turn might affect/cause increased blood pressure, heart rate, inflammation etc. (3, 19)

The behavioural explanation assumes that there might exist behavioural differences (e.g. eating habits, cancer screening, smoking prevalence etc.) between social groups which in turn contribute/cause health inequalities (3). For example, it has been reported that behaviours such as smoking and physical inactivity are less common among people with high educational attainment (20). Additionally, it has been reported that people with higher education are more likely, compared to people with lower education, to participate in screening programs, and to use primary and specialist care (20).

The explanation that points to differences in biomedical factors refers to the theory that there exist differences in biological health risk factors across social groups or individuals in a population (3). The theory focuses on the processes leading to diseases and how, psychosocial and behavioural factors affect physiological mechanisms (17).

Another important concept in health inequality research is the so-called *life course perspective* (Figure 2), which takes aspects from the other explanations into consideration. The perspective acknowledges that an individual's current health status is a result of both past and present circumstances, including effects from infancy and childhood (3).

Why do health inequalities matter?

There are different aspects on why health inequalities matter and why it is important to reduce them. A national commission for equity in health was established in 2015 by the then Swedish government. In a report from 2016 the commission states that health inequality is a problem that has to be highlighted and addressed by various actors in the community, and that the health inequalities can be seen as a problem from the perspective of the individual as well as from the society as a whole (21). Regarding the perspective of the individual there are aspects concerning moral, justice, the law and human rights. It is ethically problematic that health, which has a central role in peoples' life, systematically differs between social groups (21). In addition, health is not only an important value in itself for people, but also an important resource for other central activities in life such as work and livelihood. Many people with poorer health status (for instance manual workers) are usually more dependent on good health to be able to carry out their work and livelihood, which adds to the injustice (21). Moreover, Swedish law regulates society's obligations toward citizens and residents, and in one of the four fundament laws, the Instrument of Government, it says that society should aim for good health conditions. Due to the fact that it applies to everyone, this implies that society should strive to equalize health variations (21). Furthermore, Sweden is committed to the Universal Declaration of Human Rights, where the right to life and living standard sufficient for health and well-being is included (21). From a societal perspective resource utilisation is one aspect of importance when viewing health inequality as a problem (21). This is since the inequalities in health and premature deaths between different social groups do not only impose a substantial burden/years of life lost to the affected individuals, but also societal costs associated with loss of production, sick leave and health care (21).

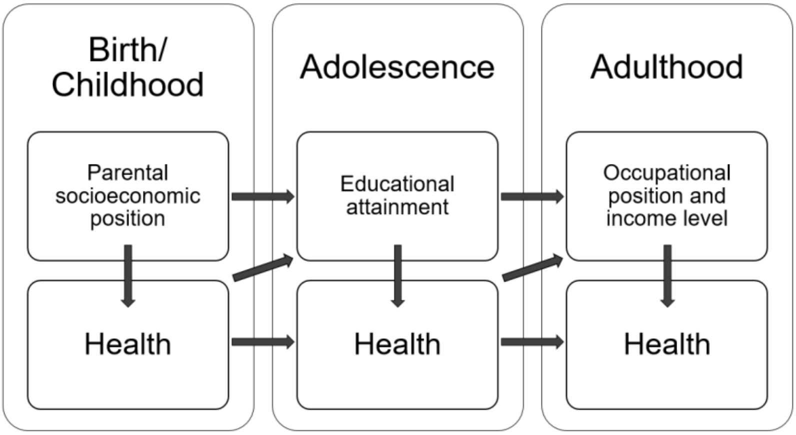


Figure 2. Image describing the life course perspective of the impact of SES on health. The image is based on image by Adler et al. (22).

Musculoskeletal disorders

Musculoskeletal disorders are diseases affecting muscles, joints, bones and connective tissues. The burden of musculoskeletal disorders is substantial (23). In 2019 approximately 1,7 billion people lived with musculoskeletal disorders and the same year musculoskeletal disorders contributed to 17% of all years lived with disability (YLDs) globally (23). Two conditions that are major contributors to the overall burden of musculoskeletal disorders are fractures and osteoarthritis (23) and this thesis focuses on these conditions.

Fractures

In 2020 approximately 103,400 fractures were registered in Sweden (24). Fractures are associated with a heavy burden on the affected individual since fractures, especially hip fractures, are associated with an increased risk of morbidity as well as mortality (25-27)

Fractures are partial or complete breaks in the bone and can be categorised as traumatic fractures, pathological fractures and stress fractures. Excessive external forces on the bone cause traumatic fractures, while pathological fractures occur in weakened bone due to pathological processes in it, such as cancer metastases and osteoporosis. Stress fractures are, on the other hand, caused by repetitive activity and overuse (28).

The type and location of fractures vary greatly based on factors related to bone quality and the trauma. Osteoporosis, which causes loss of bone mass, is a major risk factor for fractures (29). Common sites for osteoporotic fractures are the hip, spine, distal forearm and proximal humerus (30). Major modifiable risk factors involved in osteoporosis are inadequate nutritional absorption, lack of physical activity or fall risk, weight loss, cigarette smoking and alcohol consumption (31). Non-modifiable major risk factors involved in osteoporosis are history of falls, older age, female sex, white ethnic background, prior fracture and family history of osteoporosis (31).

A Swedish study by Berg et al. from 2020 (32) found that there are observable differences in fracture incidence between males and females. Males experienced osteoporotic fractures at an older age compared to females. Additionally, higher incidences regarding the majority of fractures were observed at younger ages for men than females, and this finding was suggested to be due to that young males, in contrast to young females, are more likely to take risks and experience high-energy trauma (32).

An important fracture that is well-studied is hip fracture. Hip fracture is one of the most serious bone injuries, and in Sweden in 2021, a total of 14,468 cases of hip fractures in adults were registered in the Swedish Fracture Register (33). Of these fractures, two thirds occurred among females (33). Depending on which location of the hip that is affected, hip fractures are categorised into: cervical fracture, pertrochanteric fracture and subtrochanteric fracture. In Sweden in 2021 approximately 40% of the hip fractures were cervical fractures while the pertrochanteric and subtrochanteric fractures contributed to 40% and 10% of all cases, respectively (33). The mean age for sustaining a hip fracture is 83 years (34). However, the hip fracture types vary with age. The cervical fracture is most common in the ages 40-70 years. The age distribution for pertrochanteric fracture has two peaks. The fracture is relatively common among the youngest adults and after the age of 60 its proportion increases with increasing age. What concerns subtrochanteric fractures, the largest proportion is seen in the youngest adults (33).

Hip fracture, is associated with increased mortality with mortality rate around 20-40% within one year after the time of fracture (25-27, 35-37). Post-hip fracture mortality has been reported to be associated with the following risk factors, among others: male sex, ageing, institutionalization, and the presence of co-morbidities (38).

The treatment of fractures depends, among other things, on fracture site and on what type of fracture it is. Possible treatment methods include immobilization and surgery. What concerns hip fractures, it has been suggested that early surgery (within 24-48 hours) is associated with reduced risk of mortality and morbidity (39). Since 2009 all emergency hospitals in the region of Skåne practice the so-called *Hip Line*, which is an optimised chain of care for patients with suspected hip fracture where a short time to surgery is crucial (40).

Socioeconomic inequalities in fractures and fracture-related outcomes

Socioeconomic inequalities in hip fracture incidence (41-44), post-hip-fracture care (45-47) and post-hip mortality have been reported (48, 49).

What concerns the association between fracture incidence and educational attainment as an indicator of SES, the evidence is inconsistent, where some studies have found an inverse association between hip fracture incidence and educational level (41, 42), while other studies have found no such association (50). According to a Danish study that was published in 2006, high education was associated with a lower risk of hip fractures in subjects under the age of 60 but with a higher risk in those aged 60 and older (43). Another study conducted in the United States, published in 2014, found that higher educational levels were associated with lower fracture rates in non-Caucasian females but not in Caucasian females (44).

Regarding inequalities in post-fracture care, previous studies suggest socioeconomic differences in post-hip-fracture care, where people with low SES receive less overall care and longer time to surgery (45-47).

Some previous studies have examined the association between educational attainment and post-hip fracture mortality (48, 49, 51). In an Italian study, published in 2011, early and late post-hip fracture mortality was examined in 6,896 subjects aged 65 and older. In the study, which was a prospective cohort analysis, there was no conclusive difference between patients with less than eight years of education and those with more than eight years of education in terms of post-hip fracture mortality (51). On the other hand, a Norwegian register-based study published in 2015, involving 56,269 hip fracture patients who were aged 50 and older, found an inverse association between educational attainment and post-hip fracture mortality (48). Similar to the foregoing study, a Danish population-based cohort study from 2017, involving 25,354 participants aged 65 years and older, reported that higher education was linked to significantly lower 30-day mortality after hip fracture (49).

Osteoarthritis

OA is the most common joint disease (52) and in 2019 OA was the 18th leading cause of global YLDs in people aged 50-74 years (53). In Sweden, it was estimated that in 2012, 26.6% of those aged 45 years and older had OA that had been diagnosed by a doctor (54). In the future, it is projected that the prevalence of OA will rise, and that the prevalence of doctor-diagnosed OA will reach 29.5% in 2032 (54).

OA is considered to affect the whole joint and is characterised by alterations in the articular cartilage, ligaments, subchondral bone, capsule and synovial membrane, which in turn can lead to joint failure (55). The condition can affect almost any joint, but it most often affects the knees, hips, and small joints in the hands (56). Common symptoms of OA are pain, functional impairment and decreased quality of life (52). The symptoms of OA are weakly associated with radiographic findings and vice versa (52, 57). The diagnosis of OA is made with the support of a combined assessment of anamnesis, symptoms and clinical findings (52). Imagining is an important supplement when the diagnosis is uncertain and when differential diagnoses need to be ruled out (52). OA can be categorised as primary and secondary, where the latter form can be attributed to factors such as trauma, abnormal joints at birth, surgery on joint structures etc. (55). The aetiology of OA is not fully known and both genetics as well as environmental factors contribute to the disease. According to twin studies about 47-73% and 18-53% of the variance in hip and knee OA surgery, respectively, can be attributed to genetics (58-60).

Person-level risk factors involved in OA are older age, female sex, genetics and adiposity (55). Important joint-level risk factors are joint injury, repetitive joint use and joint malalignment (55).

Treatment of OA can be divided into basic treatment, adjunctive treatment, and surgical treatment (Figure 3). According to the Swedish National Board of Health and Welfare's national guidelines, the basic treatment of OA should consist of patient education, weight reduction, exercise etc. (52). In Sweden, a physiotherapist-based intervention, known as *Artrosskola* (English translation: *OA-school)* has been implemented as a component of the national program *Better management of patients with osteoarthritis* (BOA). In the *Artrosskola* patients receive education about OA in a standardised way. BOA was initiated in 2008 and since 2010 BOA has also been a National Quality Register (https://boa.registercentrum.se/). In case of insufficient effect of the basic treatment, adjunctive treatment (e.g. pharmacologic treatment of pain) can be added. Surgical intervention is an option if the patient suffers from severe pain and significant functional impairment, where basic treatment and adjunctive treatment have not produced sufficient effect (52). About 30,000 primary knee and hip surgeries were performed due to OA in Sweden in 2019 (61, 62).

What concerns OA and mortality, some investigators have found an increased all-cause mortality in OA patients compared to the general population (63-68), however, there also exist studies that have found no such association (69-71). Moreover, studies that have focused on cause-specific mortality have reported an association between OA and higher cardiovascular mortality (64, 66, 68, 72).

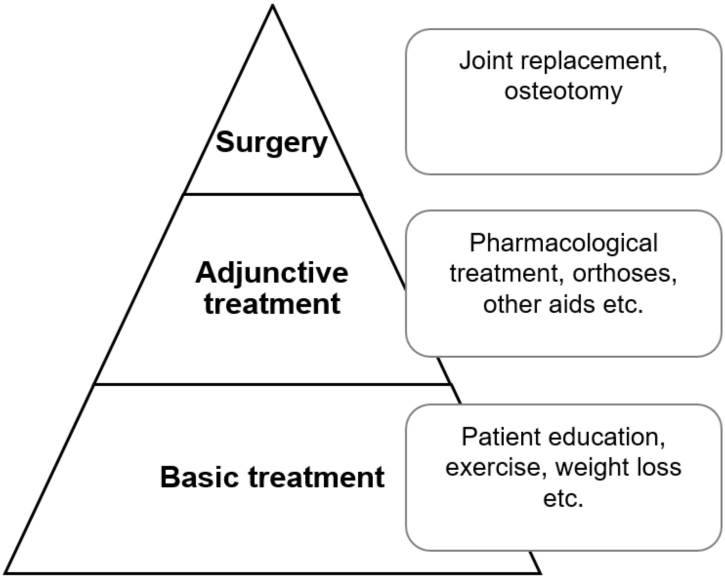


Figure 3. Image illustrating the national guidelines for OA treatment. The image is based on image by The Swedish National Board of Health and Welfare (52).

Socioeconomic inequalities in osteoarthritis and osteoarthritis-related outcomes

Studies have shown higher prevalence of OA in people with lower SES (73-77) as well as socioeconomic inequalities regarding severity/impact of OA (77-79) and OA surgery (80).

What concerns OA prevalence and SES, several studies with different indicators of SES, such as educational attainment, area-level SES and occupation, have found a higher prevalence of OA in people with lower SES (73-77).

Numerous studies have investigated the association between SES and the severity/impact of OA (77-79). A study conducted in Sweden from 2017, with educational attainment and occupation as indicators of SES, showed a socioeconomic gradient in knee pain, knee OA and health-related quality of life (77). Furthermore, an American (78) and a Finnish study (79) from 2015 and 2008, respectively, suggested similar results. The American study found that people with lower individual- and area-level SES had higher pain and lower function at the time of total knee arthroplasty in comparison with people with higher SES (78). The Finnish study showed that people with higher educational level reported lower pain scores in hip OA in comparison with people with lower educational attainment (79).

Regarding the association between SES and OA surgery, several studies have investigated the association (80-84). In a Swedish study from 2016, it was reported that lower education was associated with a higher rate of knee arthroplasty due to OA, while the results regarding hip OA were less clear (80). In addition, there exist studies that have investigated the association between SES and OA surgery but using area-based measures of SES such as neighbourhood-level income etc. (81-84).

Knowledge gaps

In order to implement preventative measures against diseases and health inequalities, it is essential to, at first, identify potential inequalities and then study underlying mechanisms and trends.

It is important to study inequalities in all-cause mortality, the burden of disease-specific mortality as well as contributing causes of deaths in order to improve public health and reduce preventable deaths. What concerns fracture-related mortality, no previous study has examined socioeconomic inequality in fracture-related mortality as a cause of death in the general population. Furthermore, no previous study has assessed socioeconomic inequalities in all-cause and cause-specific mortality among OA patients.

Since a substantial variance in OA surgery is due to environmental factors (58-60), it is important to study potential modifiable risk factors, such as socioeconomic factors, and their association with OA. As stated in foregoing section, socioeconomic inequalities in OA-related outcomes, including OA surgery, has been reported by previous research (73-80). However, previous studies have not taken potentially confounding factors such as genetics and early-life environment into account.

Moreover, even though socioeconomic inequalities in OA-related outcomes have been reported (73-80) and it is predicted that the OA burden in Sweden will rise (54), changes in prevalence and socioeconomic inequalities in knee and hip OA outcomes in Sweden over time and their contributing factors are unknown.

Aims

This thesis aims to determine the association between SES and outcomes in musculoskeletal disorders, with focus on fractures and osteoarthritis, in order to identify potential health inequalities.

Specific Aims

- To assess the absolute and relative educational inequalities in fracture-related mortality for hip fractures as well as non-hip-fractures using multiple cause of death data in the Skåne region, Sweden (Study I).
- To assess the association between education and all-cause and cause-specific mortality among OA patients, and to compare these with a sex- and age-matched cohort free of OA (Study II).
- To estimate the association between educational attainment and OA surgery using twin data from the Swedish Twin Registry (Study III).
- To examine changes in prevalence and socioeconomic inequalities in knee and hip OA surgery and non-surgery specialist care visits from 2001 to 2011 in Sweden (Study IV).

    1) How has the prevalence of knee and hip OA surgery and non-surgery specialist care visits changed and to what extent can sociodemographic factors explain the changes?

    2) How have changes in educational inequalities in knee and hip OA surgery and non-surgery specialist care visits developed and to what extent can sociodemographic factors explain the changes?

Methods

Study design and overview

The studies in this thesis are based on individual-level register data from people resident in the Skåne region, the southernmost part of Sweden (study I and II) and the whole country of Sweden (study III and IV). Study I-III are open cohort studies, while study IV has a repeated cross-sectional design. In addition, study I and III have a multiple cause of death approach and co-twin control design, respectively. The studies included are summarised in Table 1.

Educational inequalities in fracture-related mortality (study I)

To assess the absolute and relative educational inequalities in fracture-related mortality from hip and non-hip fractures in the Skåne region, a population-based open cohort study was conducted. People aged 30–99 years, resident in the region during 1998–2013 were followed until death, their 100th birthday, relocation outside Skåne, or the end of 2014. The study included people aged 30 years and older because it was assumed that most people had attained their highest level of education by this age. Data on highest level of education, marital status and country of birth was collected from the longitudinal integration database for health insurance and labour market studies (LISA) while data on age, sex, place of residence, migration- and vital status was retrieved from the Population Register.

Since fractures cannot be recorded as an underlying cause of death (UCD), a multiple cause of death approach was used, i.e. contributing causes of death on the death certificate was taken into consideration. This method was chosen since it has been reported that multiple cause of death data might provide a more accurate picture of mortality since it accounts for more factors that may be involved in death (85).

From the Swedish National Board of Health and Welfare's Cause of Death Register following information from the death certificates (Figure 4) was collected: date of death, the UCD, and up to 20 additional causes of death according to the International Classification of Diseases, 10th revision (ICD-10). We defined hip fracture-related death as a death certificate with mention of hip fractures (ICD-10 codes: S72.0–

Table 1. Overview of the four studies in this thesis	
Study I.	
Aim	To assess the absolute and relative educational inequalities in mortality from hip and non-hip fractures in the Skåne region
Study design	Register-based open cohort study with a multiple cause of death approach
Study population	People aged 30–99 years, resident in the Skåne region during 1998–2013
Data sources	Statistics Sweden, the Swedish National Board of Health and Welfare's Cause of Death Register
Main analyses	The slope index of inequality (SII) and the relative index of inequality (RII)
Study II.	
Aim	To assess the association between education and all-cause and cause-specific mortality among patients with OA in comparison to an OA-free reference cohort
Study design	Register-based open cohort study
Study population	People aged ≥45 years resident in the region of Skåne, with doctor-diagnosed OA of peripheral joints between 1998 and 2013. The reference cohort consisted of age and sex-matched references without OA diagnosis
Data sources	Statistics Sweden, the Swedish National Board of Health and Welfare's Cause of Death Register, the Skåne Healthcare Register,
Main analyses	The slope index of inequality (SII) and the relative index of inequality (RII)
Study III.	
Aim	To examine the association between educational attainment and knee and hip OA surgery using twin data
Study design	Register-based open cohort study with co-twin control design
Study population	All twins registered in the Swedish Twin Registry born between 1922 and 1980
Data sources	Statistics Sweden, the Swedish Twin Registry, the Swedish National Patient Register, the Swedish Military Conscription Registry
Main analyses	The Weibull model and Weibull within-between shared frailty model
Study IV.	
Aim	To examine changes in prevalence and socioeconomic inequalities in knee and hip OA surgery and non-surgery specialist care visits from 2001 to 2011 in Sweden
Study design	Repeated cross-sectional design
Study population	All individuals aged ≥35 years resident in Sweden between 2001 and 2011
Data sources	Statistics Sweden and the Swedish National Patient Register (by using the Swedish Interdisciplinary Panel)
Main analyses	The concentration index and the Blinder-Oaxaca decomposition method

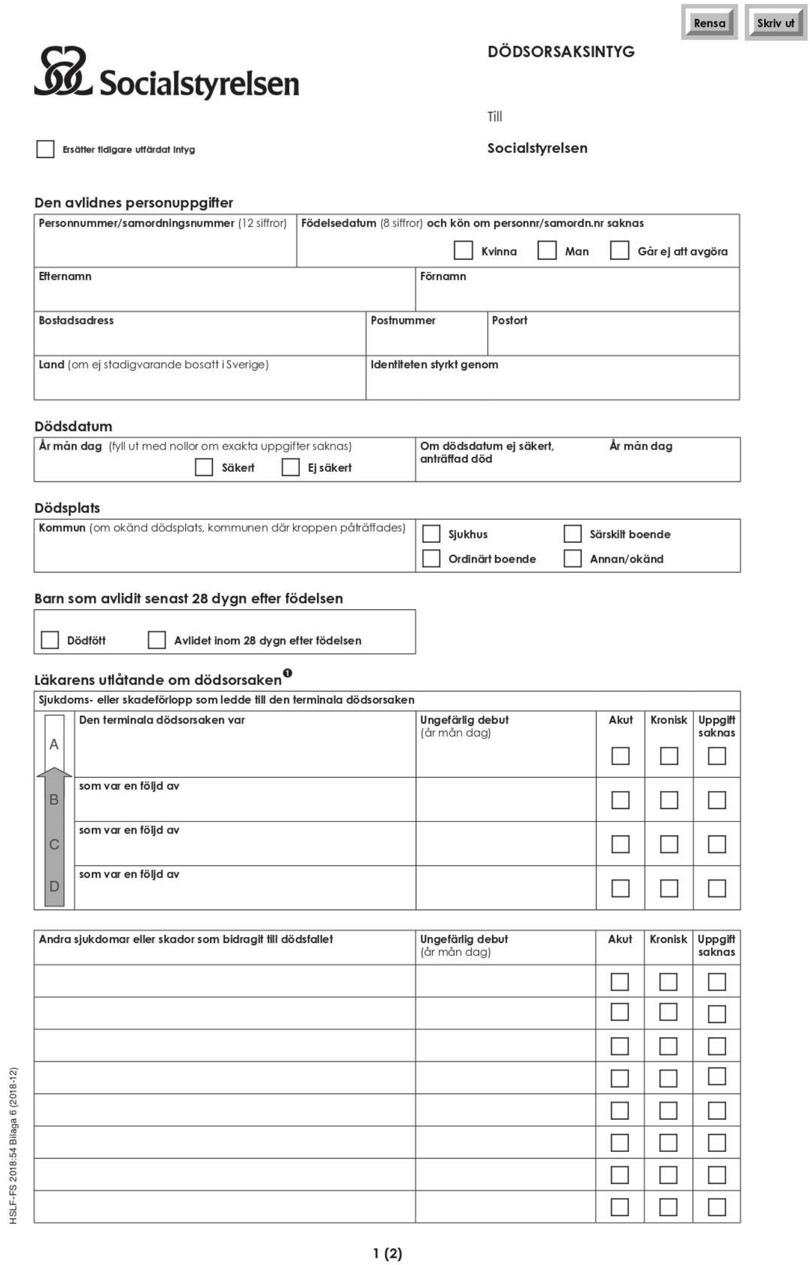
72.2, T93.1) while non-hip fracture-related death was defined as a death certificate with any mention of following ICD-10 codes: M80, S02, S12, S22.0–S22.5, S22.8–S22.9, S32.0–S32.8, S42, S52, S62, S72.3–S72.9, S82, S92, T02, T08, T10, T12, T14.2, T90.2, T91.1, T91.2, T92.1, T92.2, T93.2. The descriptions of the codes are presented in Table 2.

The level of education was classified into low (0–9 years of education), medium (10–12 years of education) and high (>12 years of education). Educational inequalities were assessed by slope and relative indices of inequality (SII and RII). Cox regression and additive hazard models were used to estimates these indices and more information about these analyses is in the section *Statistical analyses*. In the models age was used as time scale and these models were adjusted for sex, marital status (never married, previously married and married) and country of birth (Nordic born and non-Nordic born).

Educational inequalities in all-cause and cause-specific mortality in OA patients (study II)

To assess the association between education and all-cause and cause-specific mortality among patients with OA in comparison to an OA-free reference cohort in the Skåne region, a population-based open cohort study was conducted. By using data from the Skåne Healthcare Register, all residents aged ≥45 years in the region of Skåne, with doctor-diagnosed OA of peripheral joints between 1998 and 2013 were identified. The ICD-10 codes used to identify people with OA were: M15-M19, which include following groups: polyarthrosis, coxarthrosis, gonarthrosis, arthrosis of first carpometacarpal joint and the group “other arthrosis”. The last group does not include arthrosis of spine, hallux rigidus or polyarthrosis. Based on the OA cohort, an age and sex-matched reference cohort without OA diagnosis was created. The subjects of the two cohorts were followed until death, relocation outside Skåne, or the end of 2014. Individual-level data on highest level of education, marital status and country of birth was collected from LISA and data on age, sex, place of residence, migration- and vital status was retrieved from the Population Register. The National Board of Health and Welfare’s Cause of Death Register was used to retrieve the UCD and date of death reported on death certificates of the subjects who died during the observation period.

To examine cause-specific mortality the five following causes of death were used: 1) diseases of the circulatory system (ICD-10 codes: I00-I99), 2) malignant neoplasms (C00-C97), 3) mental and behavioural disorders (F00-F99) & diseases of the nervous system (G00-G99), 4) diseases of the respiratory system (J00-J99), and 5) other causes. These groups were chosen because they were the leading causes of death in the study population.



Rensa Skriv ut

Socialstyrelsen

DÖDSORSAKSINTYG

Till

Socialstyrelsen

Ersätter tidigare utfärdat intyg

Den avlidnes personuppgifter

Personnummer/samordningsnummer (12 siffror)	Födelsedatum (8 siffror) och kön om personnr/samordn.nr saknas Kvinna / Man / Går ej att avgöra	
Efternamn	Förnamn	
Bostadsadress	Postnummer	Postort
Land (om ej stadigvarande bosatt i Sverige)	Identiteten styrkt genom	

Dödsdatum

År mån dag (fyll ut med nollor om exakta uppgifter saknas) Säkert / Ej säkert	Om dödsdatum ej säkert, anträffad död	År mån dag

Dödsplats

Kommun (om okänd dödsplats, kommunen där kroppen påträffades)	Sjukhus Ordinärt boende	Särskilt boende Annan/okänd

Barn som avlidit senast 28 dygn efter födelsen

Dödfött / Avlidet inom 28 dygn efter födelsen

Läkarens utlåtande om dödsorsaken

Sjukdoms- eller skadeförlopp som ledde till den terminala dödsorsaken

		Ungefärlig debut (år mån dag)	Akut	Kronisk	Uppgift saknas
A	Den terminala dödsorsaken var				
B	som var en följd av				
C	som var en följd av				
D	som var en följd av				

Andra sjukdomar eller skador som bidragit till dödsfallet	Ungefärlig debut (år mån dag)	Akut	Kronisk	Uppgift saknas

HSLF-FS 2018:54 Bilaga 6 (2018-12)

1 (2)

Figure 4. The figure shows the first page of a Swedish death certificate (https://www.socialstyrelsen.se/en/). In the section concerning cause of death (in Swedish "Läkarens utlåtande om dödsorsaken") the underlying cause of death is described, while the section beneath is for information about contributing causes of death.

Table 2. List of ICD-10 codes with descriptions

ICD-10 code	Description of code	ICD-10 code	Description of code
Hip		**Thorax**	
S72.0	Fracture of neck of femur	S22.3	Fracture of rib
S72.1	Pertrochanteric fracture	S22.4	Multiple fractures of ribs
S72.2	Subtrochanteric fracture	S22.5	Flail chest
T93.1	Sequelae of fracture of femur	S22.2	Fracture of sternum
Pelvis and vertebrae		S22.8	Fracture of other parts of bony thorax
S12	Fracture of neck	S22.9	Fracture of bony thorax, part unspecified
S22.0	Fracture of thoracic vertebra	**Shoulder and upper limb**	
S22.1	Multiple fractures of thoracic spine	S42	Fracture of shoulder and upper arm
S32.0	Fracture of lumbar vertebra	S52	Fracture of forearm
S32.1	Fracture of sacrum	S62	Fracture at wrist and hand level
S32.2	Fracture of coccyx	T10	Fracture of upper limb, level unspecified
S32.3	Fracture of ilium	T92.2	Sequelae of fracture at wrist and hand level
S32.4	Fracture of acetabulum	**Lower limb**	
S32.5	Fracture of pubis	S72.3	Fracture of shaft of femur
S32.7	Multiple fractures of lumbar spine and pelvis	S72.4	Fracture of lower end of femur
S32.8	Fracture of other and unspecified parts of lumbar spine and pelvis Fracture of: -Ischium -lumbosacral spine, not otherwise specified -pelvis, not otherwise specified	S72.7	Multiple fractures of femur
		S72.8	Fractures of other parts of femur
		S72.9	Fracture of femur, part unspecified
		S82	Fracture of lower leg, including ancle
		S92	Fracture of foot, except ankle
T08	Fracture of spine, level unspecified	T12	Fracture of lower limb, level unspecified
T91.1	Sequelae of fracture of spine	T93.2	Sequelae of other fractures of lower limb
T91.2	Sequelae of other fracture of thorax and pelvis	**Other fractures**	
Skull		M80	Osteoporosis with pathological fracture
S02	Fracture of skull and facial bones	T02	Fractures involving multiple body regions
T90.2	Sequelae of fracture of skull and facial bones	T14.2	Fracture of unspecified body region

The level of education was classified into low (0–9 years of education), medium (10–12 years of education) and high (>12 years of education) and the inequalities in mortality were assessed by the RII and SII which in turn were estimated by the Cox model and Aalen's additive hazard model, respectively. In the models age was used as time scale and the models were adjusted for sex, marital status (never married, previously married and married) and nativity (native and non-native). Native was defined as born in Sweden with at least one Sweden-born parent, while non-native was defined as foreign-born or Sweden-born with both parents born abroad.

Association between educational attainment and knee and hip OA surgery (study III)

To examine the association between educational attainment and knee and hip OA surgery, dizygotic (DZ) and monozygotic (MZ) incomplete and complete twin pairs from the Swedish Twin Registry (STR) were identified. All twins in the STR aged 35 to 64 on the 1st of January 1987 or that turned 35 years during the follow-up were followed until OA surgery, relocation outside Sweden, death or the end of 2016. The reason to start follow-up from age 35 years and older was because it was expected that the majority of people at this age have attained their highest educational level. Moreover, OA is very uncommon before age of 35 years (86). Since most OA surgeries are done in people aged ≥ 65 years (87), people aged ≥ 65 years were excluded and instead included in a sensitivity analysis. This was done in order to minimize misclassification of the OA-surgery since people aged ≥ 65 years might already have had OA surgery before 1987.

Information on sex, zygosity, and vital status of the twins was retrieved from the STR. Data on each twin's educational attainment from the year the twin was included in the study was collected from LISA. Since LISA only has data on educational attainment from 1990, data on education from 1990 for those twins that were included during 1987 to 1989 was used. Information about knee and hip OA diagnosis and OA surgery from 1987 to 2016 was retrieved from the Swedish National Patient Register. From the Statistics Sweden's Population Register information about each twin's place of residence at age 18 and migration status was retrieved. Data on BMI and physical fitness at military conscription at the age of 18 was collected from the Swedish Military Conscription Registry. This data was available for the years 1969 to 1998 for males only, i.e. for males born between 1951 and 1980.

Knee and hip OA surgery were defined as knee (ICD-9 codes: 715, ICD-10 codes: M17) or hip OA diagnosis (ICD-9 codes: 715, ICD-10 codes: M16) registered at the same time with a knee or hip OA-related surgical procedure (arthroplasty or osteotomy). The surgery codes are based on the National Board of Health and Welfare's classification of surgical procedures from 1963 to 1996 (88) and 1997 to present (89). For knee OA surgery following surgery codes were used: 8424, 8010, 8428, 8423, 8426, NGB49, NGB19, NGK59, NGB29, NGB59, NGB53, NGB09, NGB39. Following surgery codes were used for hip OA surgery: 8414, 8010, 8409, 8419, NFB49, NFB29, NFB39, NFB99, NFK59, NFB62. For description of the surgery codes see Table 3.

The individual's highest educational attainment, which was the ranking variable, was transformed into years of education with a range from 7 to 20 years, where 7 years represented the most basic education and 20 years represented PhD education, see Table 4 regarding the transformation.

Associations between educational attainment and knee and hip OA surgery were estimated in models matched on twin pairs, using Weibull within-between (WB) shared frailty model and more information about this analysis is in the section *Statistical analyses.* Attained age was used as time-scale in the models and the models were adjusted for sex, birth cohort (1922-1934, 1935-1944, 1945-1954, 1955-1964, 1965-1980) and place of residence at age 18. For the subgroup analysis involving males born between 1951 and 1980, the models were adjusted for BMI and physical fitness at military conscription. In the subgroup analysis, males with missing data on BMI and physical fitness were excluded (N=4,136).

Changes in knee and hip OA surgery and non-surgery OA specialist care visits (study IV)

Changes in prevalence and socioeconomic inequalities in knee and hip OA surgery and non-surgery specialist care visits between 2001 and 2011 were examined using national register data and decomposition analysis. All individuals aged ≥35 years resident in Sweden between 2001 and 2011 were included, and each year from 2001 to 2011 was treated as a cross-section. The lower age limit was based on that it was assumed that the majority of people at this age have attained their highest educational level. The Swedish Interdisciplinary Panel (SIP), which contains information from several official registers, was used to collect individual-level data. Following variables were included into the decomposition analysis: sex (female, male), age (as a continuous variable), country of birth (Sweden-born, foreign-born), civil status (never married, married/registered partnership, previously married/in a partnership), employment (employed, unemployed or not in the labour force), disposable income (five groups based on quintiles), highest educational attainment of mother and father, respectively (>9 years of education, <10 years of education, missing information about education). Country of birth of parents was also included and this variable was categorised as Sweden-born if both parents were born in Sweden and as foreign-born for any other scenario (Sweden-born parents, foreign-born parents, missing information about parents' country of birth).

Table 3. Surgery codes used for knee and hip OA surgery	
Code*	**Description of code**
Knee OA surgery	
8424	Bicompartmental knee arthroplasty
8010	Osteotomy
8428	Tricompartmental knee arthroplasty
8423	Unicompartmental knee arthroplasty
8426	Insertion of patellar prosthesis
NGB49	Primary total prosthetic replacement of knee joint using cement
NGB19	Primary partial prosthetic replacement of knee joint using cement
NGK59	Angulation, rotation or displacement osteotomy of knee or lower leg
NGB29	Primary total prosthetic replacement of knee joint not using cement
NGB59	Primary prosthetic interposition arthroplasty of knee joint
NGB53	Primary patellofemoral prosthesis
NGB09	Primary partial prosthetic replacement of knee joint not using cement
NGB39	Primary total prosthetic replacement of knee joint using hybrid technique
Hip OA surgery	
8414	Total prosthetic replacement of hip joint
8010	Osteotomy
8409	Other related surgeries (hip arthroplasty without using foreign material)
8419	Other related surgeries (hip arthroplasty using foreign material)
NFB49	Primary total prosthetic replacement of hip joint using cement
NFB29	Primary total prosthetic replacement of hip joint not using cement
NFB39	Primary total prosthetic replacement of hip joint using hybrid technique
NFB99	Other primary prosthetic replacement of hip joint
NFK59	Angulation, rotation or displacement osteotomy of femur
NFB62	Primary prosthetic replacement of joint surface of femoral head

* The surgery codes are based on the National Board of Health and Welfare's classification of surgical procedures from 1963 to 1996 (88) and 1997 to present (89).

Table 4. Definition of years of education		
Statistics Sweden's SUN 2000	**Statistics Sweden's description of the code**	**Years of education in study**
<200	Pre-secondary education shorter than 9 years	7
≥200 and <300	Pre-secondary education of at least 9 years	9
>300 and <320	Secondary education of at least one semester (but not 2 years)	10
≥320 and <330	Secondary education at least 2 years (but not 3 years)	11
≥330 and <400	Secondary education of 3 years	12
≥410 and <500	Postsecondary education of at least one semester (but not 2 years)	13
≥520 and <530	Postsecondary education of at least 2 years (but not 3 years)	14
≥530 and <540	Postsecondary education of at least 3 years (but not 4 years)	15
≥540 and <550	Postsecondary education of at least 4 years (but not 5 years)	16
≥550 and <600	Postsecondary education of 5 years or longer	17
≥600 and <640	Other / unspecified research education and Licentiate degree	18
640	PhD education	20

The individual's highest educational attainment, which was the ranking variable, was transformed into years of education with a range from 7 to 20 years, where 7 years represented the most basic education and 20 years represented PhD education, see Table 4 regarding the transformation.

Knee and hip OA surgery were defined as knee (ICD-10 codes: M17) or hip OA (ICD-10 codes: M16) registered as the main diagnosis at the same time as a knee or hip OA-related surgical procedure (arthroplasty or osteotomy) was registered. For knee OA surgery we used the following surgery codes: NGB49, NGB19, NGK59 NGB29, NGB59, NGB53, NGB09, and NGB39. Following surgery codes were used for hip OA surgery: NFB49, NFB29, NFB39, NFB99, NFK59, and NFB62. The surgery codes are based on the National Board of Health and Welfare's classification of surgical procedures (89) and for description of the codes see Table 3. Knee and hip OA non-surgery specialist care visits were defined as knee (ICD-

10 codes: M17) or hip OA (ICD-10 codes: M16) registered as the main diagnosis without OA-related surgical procedure registered at the same time.

People with more than one OA surgery and/or non-surgery specialist care visit in a year were only counted once per year.

The concentration index was used to assess educational inequality in knee and hip OA surgery and non-surgery specialist care visits. The Blinder-Oaxaca decomposition method was used to examine changes in prevalence and educational inequalities of the OA outcomes between the two years 2001 and 2011. More information about the concentration index and decomposition analysis is in the section *Statistical analyses.*

Data sources

Statistics Sweden

Statistics Sweden is a government agency responsible for official statistics. LISA, which is maintained by Statistics Sweden, was used to retrieve information about the subjects' educational level, marital status, country of birth, income and employment. LISA integrates data from social and educational sectors as well as from the labour market. The database contains data from the year 1990 and forward on all people aged 16 or older (from the year 2010 people aged 15 are also included) who were registered in Sweden on 31 and December each year (https://scb.se/en/).

The Population Register from Statistics Sweden was used to collect information about the subject's age, sex, place of residence, migration- and vital status.

The data provided by Statistics Sweden is of good quality and the quality of the official statistics is evaluated annually (https://scb.se/en/).

The National Board of Health and Welfare

The National Board of Health and Welfare is a government agency under the Ministry of Health and Social Affairs and is responsible for developing statistics, regulations, and knowledge for the government, health care workers, and social service providers (https://www.socialstyrelsen.se/en/). The National of Health and Welfare's Cause of Death Register was used to retrieve the underlying and additional causes of death in study I and II. The register is considered to be reliable with a high coverage (90).

Information about OA surgery and specialist care visits for study III and IV was retrieved from the National Patient Register, which is maintained by The National Board of Health and Welfare. The Swedish National Patient Register covers inpatient data from 1987. Outpatient specialist care data is available from 2001 and covers, among others, day surgery from private and public caregivers (https://www.socialstyrelsen.se/en/). The reliability of the register is considered to be good and reflects the data available in the regional patient administrative systems (91).

The Skåne Healthcare Register

The Skåne Healthcare Register (SHR) was used in study II to identify people with doctor-diagnosed OA. SHR is a regional healthcare register that contains data on all medical consultations, both public and private, in the Skåne region from 1998 onwards. The administrative body of Region Skåne (the regional council of Skåne) is the data controller of SHR. The register is consider to have good coverage and reliable data (92).

The Swedish Twin Registry

In study III the Swedish Twin Registry (STR) was used to identify complete and incomplete mono- and dizygotic twin pairs. The STR is managed by the Karolinska Institute and is the largest twin cohort in the world containing approximately 85,000 Sweden-born twin pairs.

The Swedish Military Conscription Registry

The Swedish Military Conscription Register was used in study III to retrieve information about physical fitness and BMI at conscription. The register is managed by The Swedish Defence Conscription and Assessment Agency and contains data on approximately 2 million people between 1969 and 2018. The register covers about 90% of men born between 1951 and 1988 (93).

The Swedish Interdisciplinary Panel

For paper IV data from the Swedish Interdisciplinary Panel (SIP) was used. The SIP is a database hosted at the Centre for Economic Demography at Lund University and it contains data from several official registers including Statistics Sweden's Population Register and LISA as well as The Swedish National Patient Register. By using the Statistics Sweden's multi generation register in SIP it was possible to link parent to child and thus get information about country of birth and educational level of parents.

Statistical analyses

Age-standardised mortality rate and rate ratio

Age-standardised mortality rates and rate ratio (RR) were calculated in study I. Age-standardised mortality rates, i.e. the mortality rate adjusted to a standard age distribution, were computed with the direct method, using the Swedish population in the year 2000 as the standard population. The rate ratio (RR) was calculated as the ratio of age-standardised mortality rate in the group with low level of education divided by the rate in the group with high level of education.

Hazard ratio

Hazard ratios (HR) were estimated in study I and study III. The method for obtaining the HR in study III is presented under the heading *Twin data analysis*, while the method used in study I will be presented in this section. HR is an estimate of the ratio of hazard rates of two groups, where hazard is the probability that a certain event will occur at a certain time (small time interval), given that it has not occurred before (94). In study I, HR was estimated by using the Cox proportional hazards model, which is a regression model frequently used in survival analysis (94). Schoenfeld's residuals plot was used to examine the proportional hazards assumption. In order to fulfil the assumption, the study population had to be divided in three and two different age strata when analysing hip fractures and non-hip fractures, respectively.

Slope and relative index of inequality

Slope index of inequality (SII) and relative index of inequality (RII) were used to measure the absolute and relative educational inequalities in mortality in study I-II. The SII measures the absolute difference in health status or health problem frequency between the hypothetical best-placed and worst-placed person, ranked by socioeconomic status. The RII is, on the other hand, the ratio of the health status or health problem frequency in the two extremes (95, 96). The measurements are sensitive to the population size within the different socioeconomic groups, which may change over time. To generate the SII and the RII the educational groups were ordered from highest to lowest level of education. Then the population of each educational group was given a fractional rank, which was based on the midpoint of its range in the cumulative distribution in the population (95, 96). As an example, if a population consist of 20% with high education, 30% with medium education and 50% with low education, the educational groups will be given the following fractional ranks: high education 0.10 (0.2/2), medium education 0.35 (0.2+(0.3/2)), and low education 0.75 (0.2+0.3+(0.5/2)). The mortality was then regressed against the fractional rank of the different educational groups by using Aalen's additive hazard model for SII and Cox model for RII, while age was used as time-scale. The estimated coefficient of the fractional rank from additive hazard model yields an estimate of SII and the exponential of the estimated coefficient of the fractional rank from Cox model provides an estimate of RII. R-codes from Moreno-Betancur et al. (96) were used to perform the analyses. The indices were adjusted for sex, marital status and country of birth.

Twin data analysis

Twin data was analysed in study III in order to examine the association between educational attainment and knee and hip OA surgery. We used a co-twin control design where twins were treated as pairs matched on familial confounders like genetics and early-life exposures such as parental characteristics.

We performed both analyses that were unmatched and matched on twin pairs in order to examine the association between education and the outcomes. We assumed that the potential discrepancy between the unmatched and matched estimates were due to the impact of shared genetics and early-life environment (97). The associations were assessed by estimating HRs using Weibull models and the HRs were reported per 3 years of education.

For the unmatched analyses, unmatched twin pairs that included both incomplete and complete DZ and MZ twin pairs were treated as a cohort. In the matched analyses we used the gamma-Weibull within-between (WB) shared frailty model (98) using Mundlak specification. For the WB analyses we used the R-code provided by Dahlqwist et.al (98). In sibling comparison research, WB models are well-established and used to separate the association between exposure and outcome into a "within-cluster effect" and a "between-cluster effect" (97). MZ twins share many potential confounders (100% of their genes (99) and their early-life environment), and when assuming no individual level confounders, the within effect in MZ twin pairs represents a direct causal effect of educational attainment on OA surgery. In the study, the “between-cluster effect” quantified the degree of shared familial confounding in the association between the exposure and the outcome (97) and a “between-cluster effect” different from zero implied the presences of shared familial confounding (97).

In the analyses we assessed DZ and MZ twin pairs combined, and DZ and MZ twin pairs separately. Since MZ twins share 100% of their genes, while DZ twins share, on average, 50% of their genes (99), any difference between the DZ and MZ estimates were assumed to reflect potential confounding by genetic factors.

Besides using Weibull models, we also did analyses using the Cox model and stratified Cox model. In addition, we also performed analyses treating educational attainment as a binary variable (presented in the supplementary material of study IV). Plots of Schoenfeld residuals were used to evaluate the proportional hazard assumption.

Confounders

A confounder is associated with the exposure and also independently associated with the outcome (94).

Based on previous research we considered age (13, 14, 38), sex (13, 14, 38), marital status (100-105) and country of birth/nativity (1, 15) as confounders in study I and II.

Besides age (13, 14, 55) and sex (13, 14, 55), we also considered birth cohort, and early-life place of residence (106, 107), BMI (55, 108-110) and physical fitness (111-114) as confounders in study III.

The concentration index

In study IV, the concentration index was used to assess educational inequality in the outcomes. The concentration curve serves as the foundation for the concentration index. The concentration curve is created by graphing the cumulative proportion of the population (X-axis) ranked by socioeconomic indicator against the cumulative proportion of the desired outcome variable (Y-axis) (115, 116). When the share of the outcome variable is on the y-axis the results represent the Relative Concentration Index (RCI). The concentration curve will be a 45-degree line, running from the bottom left corner to the top right corner, if there is no educational inequality in outcome. This line is known as the line of equality (Figure 5). The area between the concentration curve and the line of equality, multiplied by two, is the RCI. If the concentration curve lies above (below) the 45-degree line, then the value of the RCI is negative (positive) suggesting greater concentration of the outcome among the low (high) SES groups. The magnitude of the RCI ranges from -1 to 1, with a higher absolute value suggesting greater inequalities. However, Wagstaff (117) showed that the range of RCI is not between -1 and +1 when the health outcome variable is bounded (e.g. binary outcomes). To overcome this, Wagstaff suggested the normalization of the RCI, known as the Wagstaff Index (WI). Using the RCI, one can calculate Absolute Concentration Index (ACI) by multiplying the RCI by the mean of health outcome variable (107, 108). Stata's *conindex* function was used to estimate the WI and ACI (118).

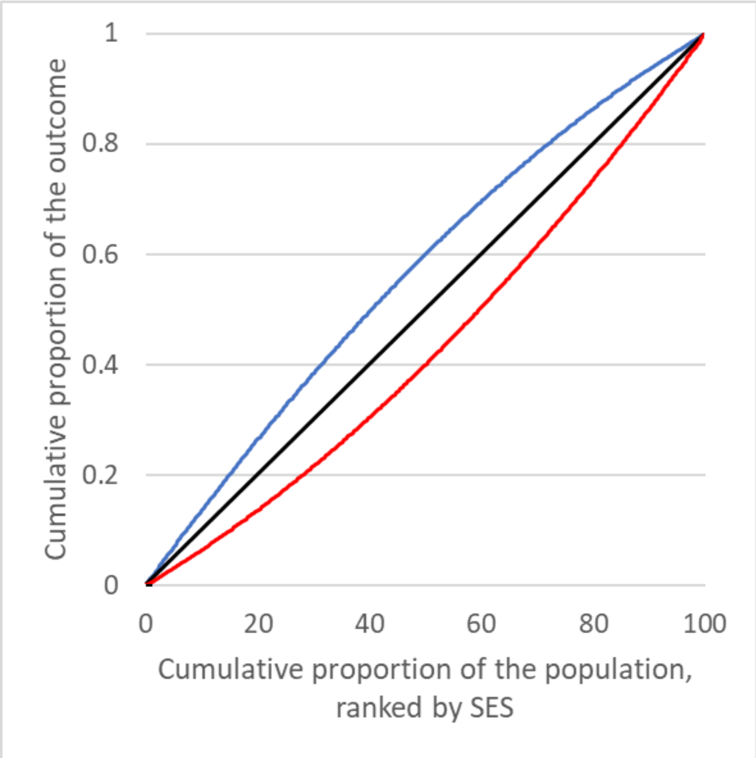


Figure 5. Image illustrating the line of equality (black line) and two concentration curves. The blue line represents a concentration curve where the outcome is more concentrated among people with lower SES. In contrast, the red line represents a concentration curve where the outcome is more concentrated among people with higher SES.

Decomposition analysis

In study IV, the Blinder-Oaxaca decomposition method (119, 120) was used to examine changes in the knee and hip OA outcomes. The decomposition method explains the difference in the means of an outcome variable between two groups and the method was developed in 1973 by Blinder and Oaxaca and originally used to examine labour-market outcomes by groups based on sex and race (119, 120). Besides being applied in labour market studies, the method can also, among others, be used to examine health inequalities (121).

What concerns study IV, the Blinder-Oaxaca decomposition was used to examine changes in prevalence and relative educational inequalities (measured by WI) in knee and hip OA surgery and non-surgery specialist care visits between 2001 and 2011. By using the method, it was possible to determine how much of the changes between 2001 and 2011 that were attributed to differences in the sociodemographic characteristics of the populations (i.e. the explained part), versus differences in the sociodemographic characteristics' coefficients and unmeasured factors (i.e. the unexplained part) (119, 120). With the population of 2001 as a reference, we computed the decomposition from the perspective of the population of 2011. Consequently, we assessed what the prevalence and inequalities would have been if the population of 2011 had the same sociodemographic characteristics and coefficients as the population of 2001.

We used the *oaxaca* function in Stata to examine changes in prevalence and since the outcomes were binary we used logit model (122).

The Wagstaff method developed by Wagstaff et al. (123) has been the most commonly used method to decompose socioeconomic inequalities (121). However, the approach has limitations. The decomposition method is one-dimensional and focuses on health but not on rank. Thus, it describes the degree of variation in health rather than accounting for the covariance between rank and health (121, 124). There exists other decomposition methods that are two-dimensional and that estimate both health and rank (121, 124), however they are, as the Wagstaff method, limited to only decompose one form of rank dependent index correctly (121). In order to decompose WI in study IV, a recentered influence function (RIF) decomposition method, developed by Heckley et al. (121), was used. Influence functions (IFs) are statistical tools used for analysing the robustness of distributional statistics (125). The RIF decomposition method uses RIF regression. RIFs, which are a special type of IFs, are tools used to examine the impact distributional changes of the exposure variable has on the distribution of the outcome variable (125). The *oaxaca_rif* function in Stata (125) was used to perform the RIF decomposition.

Statistical analysis software

R is an open-source software environment for statistical computing and graphics (https://www.r-project.org), and it was used to perform the main statistical analyses in study I-III. For the main analyses in study IV the statistical software *Stata* was used (https://www.stata.com).

Ethical considerations

Since the studies in this thesis involves sensitive data, the studies required approval from an ethical review board before study start (in accordance with the Swedish Ethical Review Act (SFS 2003:460)). The studies were approved by the Regional Ethics Committee in Lund. Study I and II were approved by the diary number 2014/276, while study III and IV were approved by diary numbers 2017/115 and 2012/03, respectively. The data used was stored and managed according to current regulations.

Results

Educational inequalities in fracture-related mortality (study I)

In study I, 999,148 people were included after excluding 70,337 people (6.6%) with unknown educational attainment, 88 people with missing country of birth, and 72 people with both unknown educational attainment and missing country of birth. A total of 5,121 fracture-related deaths (2.9% of all deaths) were identified during a mean follow-up of 12.2 years. 3,110 (1.8% of all deaths) of the total number of fracture-related deaths were associated with hip fracture. About 50.8% of the included people were females and a majority of the people were Nordic-born and married. Characteristics of the study population are presented in Table 1 in Study I.

Hip fracture-related mortality

As the educational level decreased the age-standardised, hip fracture-related mortality rates increased (Figure 1, Study I). The age-standardised, hip fracture mortality rates were 31 (95% CI: 30, 32) and 23 (95% CI:20, 26) per 100,000 person-years in people with low and high educational attainment, respectively (representing an RR of 1.4 (95% CI: 1.2, 1.5)). The corresponding mortality rates were 37 (95% CI: 35, 40) and 28 (95% CI: 23, 34) for males (RR 1.3 (95% CI: 1.1, 1.5)) and 28 (95% CI: 26, 29) and 19 (95% CI: 15, 23) for females (RR 1.5 (95% CI: 1.3, 1.7)). The HRs showed increased risk of hip fracture-related deaths in people with a low versus high educational attainment in all age- and sex groups except females aged 30–69 and males aged ≥85 years (Table 2, Study I). People younger than 85 years with a medium level of education generally had a higher hip fracture mortality risk compared with those with high-educational attainment, while the results concerning the oldest age strata were inconclusive. Table 5 presents the results concerning RII and SII. The relative inequalities, measured by the RII, ranged from 3.5 (95% CI: 1.7, 7.3) in the youngest age group to 1.3 (95% CI:1.1, 1.6) in those aged ≥85 years. The absolute inequalities, measured by the SII, showed that among people aged 30–69 years, there was about one more hip fracture-related death per 100,000 person-years in the least educated compared with the most educated individuals, SII =1.4 (95% CI: 0.6, 2.1). The corresponding numbers in age group 70-84 and in the oldest age group were approximately 33 (95% CI: 20, 46) and 110 (95% CI: 26, 195), respectively.

Table 5. Slope index of inequality (SII) and relative index of inequality (RII) in hip fracture-related mortality		
	Inequality measures	
	SII [a]	RII
30-69 years		
All	1.4 (0.6, 2.1)	3.5 (1.7, 7.3)
Males	2.1 (0.9, 3.3)	5.1 (2.0, 13.2)
Females	0.5 (-0.5, 1.6)	1.9 (0.6, 6.0)
70-84 years		
All	33.0 (20.3, 45.7)	1.8 (1.5, 2.3)
Males	45.6 (26.6, 64.6)	2.1 (1.5, 2.9)
Females	21.0 (4.8, 37.3)	1.5 (1.1, 2.2)
85+ years		
All	110.0 (25.5, 194.5)	1.3 (1.1, 1.6)
Males	23.8 (-122.9, 170.4)	1.0 (0.8, 1.4)
Females	151.8 (50.9, 252.8)	1.5 (1.1, 1.9)

[a] per 100,000 person-years

Non-hip fracture-related mortality

The age-standardised non-hip fracture-related mortality rates were 20 (95% CI: 18, 21) and 16 (95% CI: 14, 19) per 100,000 person-years in people with a low and high educational attainment, respectively, representing a RR 1.2 (95% CI: 1.0, 1.4). The RR was 1.4, (95% CI: 1.1, 1.6) for males and 1.1 (95% CI: 0.8, 1.3) for females (Figure 2, Study I). Table 6 presents the results concerning RII and SII. The RII showed that among people aged 30–69 years, the risk of non-hip fracture-related mortality was 2.4 times higher (95% CI: 1.6, 3.4) for those with the lowest compared with those with the highest educational attainment. The results concerning absolute and relative educational inequality among people aged ≥70 years were inconclusive. The SII showed that there were about 4 (95% CI: 2, 6) more non-hip-fracture deaths per 100,000 person-years in people with the lowest versus the highest educational attainment among those aged 30–69 years. The difference was more noticeable in males than in females.

Table 6. Slope index of inequality (SII) and relative index of inequality (RII) in non-hip fracture-related mortality		
	Inequality measures	
	SII [a]	RII
30-69 years		
All	3.9 (2.2, 5.5)	2.4 (1.6, 3.4)
Males	5.1 (2.6, 7.7)	2.3 (1.5, 3.5)
Females	2.4 (0.6, 4.2)	2.4 (1.2, 4.8)
70+		
All	8.1 (-4.7, 20.9)	1.2 (0.9, 1.4)
Males	15.6 (-2.4, 33.7)	1.3 (1.0, 1.9)
Females	2.1 (-16.6, 20.8)	1.0 (0.8, 1.3)

[a] per 100,000 person-years

Educational inequalities in all-cause and cause-specific mortality in OA patients (study II)

In study II, a total of 123,993 people were included in the OA-cohort (60.9% females) after excluding 4,195 people with unknown educational attainment, five people with unknown nativity, and four people with missing UCD. The final reference cohort consisted of 121,318 people (60.7% females) after 2,671 with unknown educational attainment and four people with unknown nativity were excluded. The mean age at study entry was 66.6 (SD=11.6) for the OA cohort and 66.5 (SD=11.6) years for the reference cohort. The mean follow-up time was 7.1 years for the OA cohort and 6.6 years for the reference cohort. During follow-up, 24,493 and 28,843 deaths were identified in the OA and reference cohorts, respectively. Characteristics of the study population are presented in Table 1 in Study II.

The relative educational inequality, measured by the RII, showed that the all-cause mortality rate was approximately 1.5 times higher in those with the lowest compared with those with the highest educational attainment.in both the OA (Table 2, Study II) and reference cohorts (Table 3, Study II) (OA cohort: RII 1.53, 95% CI: 1.46, 1.61; and reference cohort: RII 1.54, 95% CI: 1.47, 1.62). The absolute educational inequalities, measured by the SII, showed that there were 937 (95% CI: 811, 1063) more all-cause deaths per 100,000 person-years in the lowest vs. highest educated OA patients (Table 2, Study II). The corresponding figure was greater in the reference cohort, where there were 1,265 (95% CI: 1109, 1421) more deaths per 100,000 person-years in favour of the highest-educated, (Table 3, Study II). Additionally, females and individuals aged 45-74 were found to have greater absolute educational inequalities in all-cause mortality in the reference cohort than in the OA cohort.

Higher mortality was observed in patients with lower education in both cohorts for all specific causes (even though the confidence interval included the null value of 1 for the cause *Mental and behavioural disorders & Diseases of the nervous system*). Across all subgroups in both cohorts, educational inequalities in favour of the more highly educated were generally seen. The magnitudes of relative inequalities were generally comparable between the OA and reference cohorts. Greater absolute educational inequalities for *Malignant neoplasm* (subjects aged ≥45, females, and subjects aged 45-74 years) and Diseases of the respiratory system (subjects aged ≥45 and subjects aged 45-74 years) were seen in the reference cohort in comparison to the OA cohort.

Subgroup analyses based on OA type showed that the relative and absolute educational inequalities in mortality were similar in subjects with knee and hip OA (Table 2, Study II)

Figure 6 shows the contribution, in percentage, of specific causes of death to the absolute educational inequality in all-cause mortality. Generally, *Diseases of the circulatory system* contributed the most, and *Mental and behavioural disorders & Diseases of the nervous system* contributed the least, to the absolute educational inequality in all-cause mortality in both the OA and reference cohorts. The only exception was in subjects aged 45-74 years in the reference cohort, where *Malignant neoplasm* contributed the most (37.1%) to the absolute educational inequality. While deaths from *Malignant neoplasm* tended to contribute more to the absolute educational inequality in mortality in the reference cohort, diseases of the circulatory system tended to have a higher contribution in the OA cohort compared to the reference cohort. Contrary to what was shown for cancer-related mortality, the contribution of cardiovascular death increased with age.

Figure 6. Contribution (%) of specific causes of death to the absolute educational inequality in all-cause mortality in the OA- and reference cohort.

Association between educational attainment and knee and hip OA surgery (study III)

In study III, a total of 67,071 twins (53.7 % females) were included after excluding 1,077 people with unknown educational attainment and 1,396 people with missing information about place of residence at age 18. The study sample consisted of 18,784 DZ and 8,657 MZ complete twin pairs, and 12,189 twins without a co-twin. The mean age at study entry was 41.7 (SD=8.7) and the mean follow-up was 22.6 years for both knee and hip OA surgery. During the follow-up, a total of 2,017 knee OA surgeries and 2,285 hip OA surgeries were identifies. Characteristics of the study population are presented in Table 1 in Study III.

Knee OA surgery

The unmatched analysis of the total sample, generated by the Weibull regression model, showed a hazard ratio (HR) of 0.90 (95% CI: 0.86, 0.95) for knee OA surgery, indicating that for every three additional years of education the rate of knee OA surgery lowers by ~10%. When adjusting for familial confounding through twin design the results showed a HR of 1.05 (95% CI: 0.95, 1.16) suggesting potential familial confounding which is also supported by the “between-effect estimates”. Comparing HRs from DZ and MZ twins suggested that the association between education and knee OA surgery is mainly confounded by genetic factors. The estimate for MZ twins was 1.06, with a 95% confidence interval of 0.81 to 1.32, suggesting no association between the individual’s education and the risk of knee OA surgery. What concerns the between-pair estimates, the HR for the MZ twins was 0.71 (95% CI: 0.41, 1.01). The finding suggests that there exists familial confounding on the association between educational attainment and knee OA surgery (Figure 7). When individuals aged 65 years and older were included, the findings were similar (Supplementary material Study III, Figure A1).

The estimates indicated neither an association between educational attainment and OA surgery, nor a familial confounding on the association when treating education as a binary variable (Supplementary material Study III, Figure A2-A3). When education was treated as a binary variable rather than a continuous variable, estimates produced by the Cox and stratified Cox models suggested that education had a protective effect on the association (Supplementary material, Figure A5).

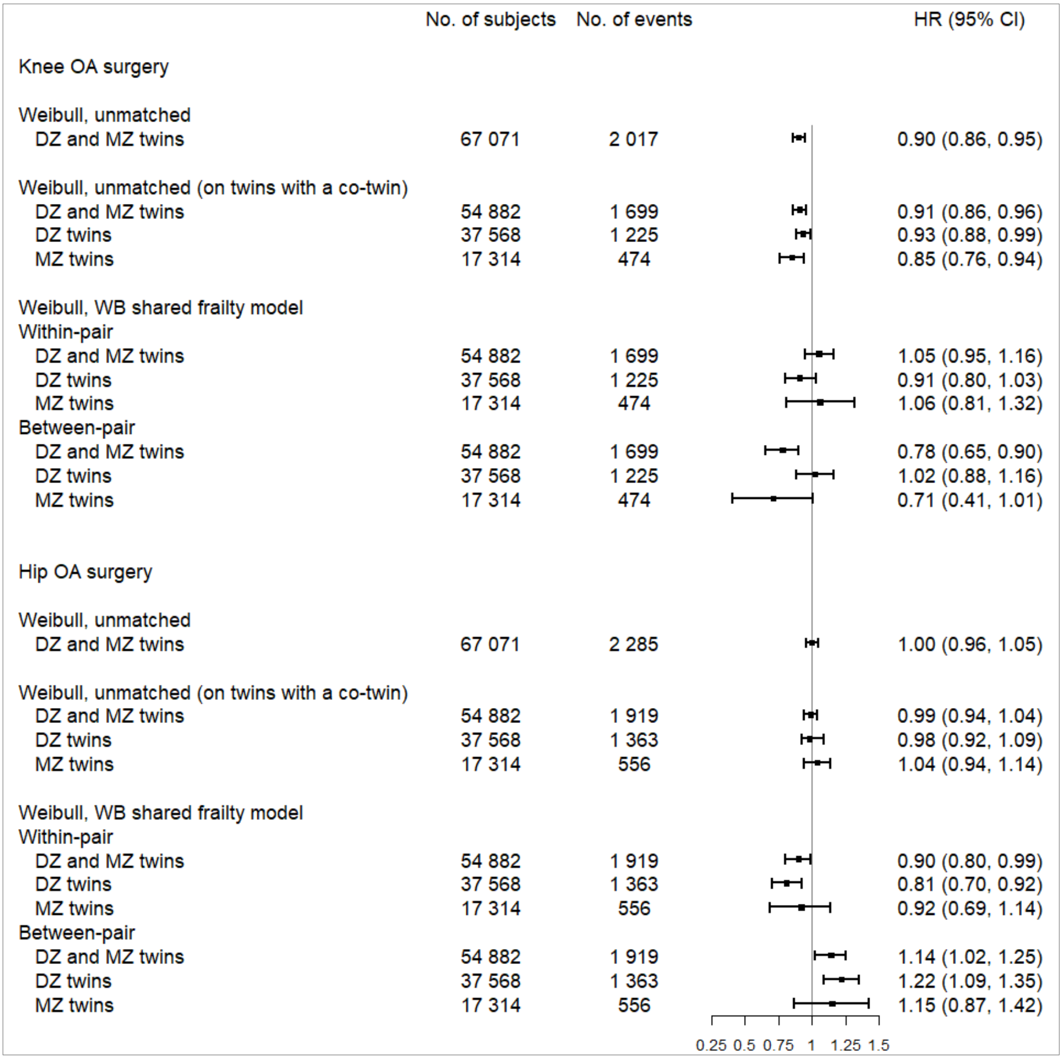


Figure 7. The hazard ratios (HR) per 3 years of education with 95% confidence intervals (CI) for knee and hip OA surgery, for unmatched and matched dizygotic (DZ) and monozygotic (MZ) twins.

Hip OA surgery

The unpaired analysis's HR for hip OA surgery for the total sample was 1.00 (95% CI: 0.96, 1.05). After accounting for matching, the estimate was 0.90 (95% CI: 0.80, 0.99) for total sample, and 0.81 (95% CI: 0.70, 0.92) and 0.92 (95% CI: 0.69, 1.14) among DZ and MZ twins, respectively. The between-pair estimate in MZ twin pairs (HR: 1.15, 95% CI: 0.87, 1.42) was inconclusive with respect to the size of confounding from familiar shared factors (Figure 7). Similar results were seen when people aged 65 years and older were included, when education as a binary variable was used, and when Cox and stratified Cox model were used (Supplementary material Study III, figure A1-A5).

Adjustment for BMI and physical fitness

For males whom data on BMI and physical fitness was available (males born 1951-1980), the unadjusted within-twin estimate for knee OA surgery showed a HR of 0.36 (95% CI: 0.00, 1.98) in MZ twins (Figure 2, Study III). Although this estimate remained similar after adjusting for BMI, physical fitness, birth cohort, and residence at age 18, suggesting no relevant confounding from BMI and physical fitness, the CIs were broad, precluding us from drawing firm conclusions.

After adjusting for BMI and physical fitness, the within-twin estimates for hip OA surgery for MZ twins remained largely unchanged with point estimates between 1.54 and 1.64. (Figure 2, Study III).

Changes in knee and hip OA surgery and non-surgery specialist care visits (study IV)

A total of 4,794,693 (51.4% females, mean (SD) age 55.8 (13.9)) and 5,359,186 (51.1% females, mean (SD) age 57.3 (14.4)) people were included for the years 2001 and 2011, respectively. In 2001, there were 5,628 knee OA and 7,895 hip OA surgeries. The corresponding numbers for 2011 were 11,477 and 12,442, respectively. What concerns non-surgery specialist care visits, in 2001 there were 17,360 visits with knee OA as the main diagnosis and 8,988 with hip OA. In 2011 the corresponding numbers were 33,184 and 13,688, respectively. Descriptive statistics of the study populations are presented in Table 1, Study IV.

Changes in prevalence

Figure 8 presents changes in prevalence of the outcomes between 2001 and 2011. Compared to 2001, the prevalence of all outcomes was greater in 2011 (Table 2, Study IV). In 2011 compared to 2001, there were 97 (95% CI: 91.8, 101.8) more knee OA surgeries per 100,000 people. About 43.6% of this difference in prevalence was attributed to differences in the populations' characteristics, i.e. explained, while approximately 56.4% of the difference was attributed to differences in the sociodemographic characteristics' coefficients and unmeasured factors, i.e., unexplained. Differences in age, parents' country of birth, parents' educational attainment, civil status and individual educational attainment contributed the most to the explained part.

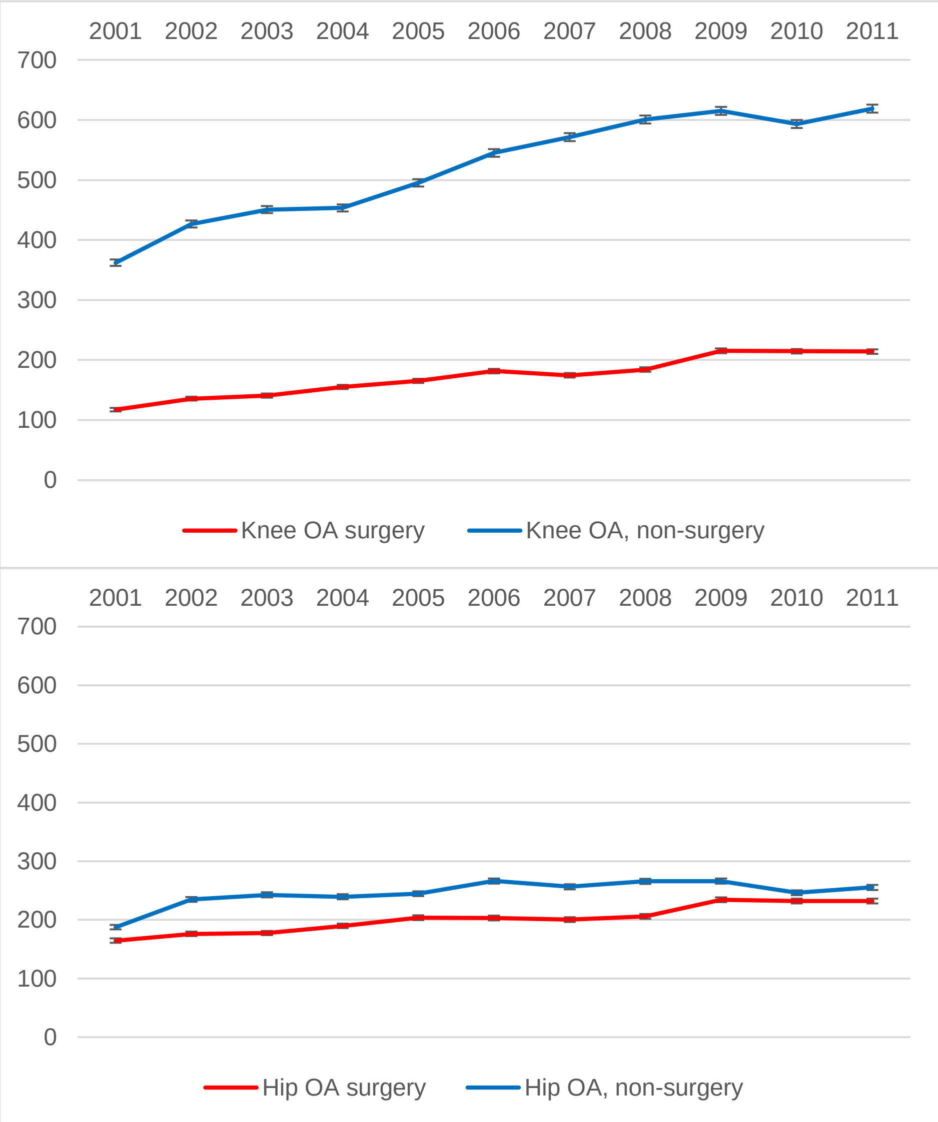


Figure 8. Number of knee and hip OA surgeries and non-surgery specialist care visits per 100,000 people, with 95% confidence intervals, for each year from 2001 to 2011. The numbers reflect the number of people having at least one of the studied outcomes per year.

While differences in the three latter variables contributed to a decline in prevalence, differences in the three former variables contributed to an increase in prevalence. What concerns the unexplained part of the decomposition, age and educational attainment contributed to an increase in prevalence, whereas country of birth contributed to a decline in prevalence. Unmeasured factors also contributed considerably to the unexplained part. Regarding knee OA non-surgery visits, there were approximately 257 (95% CI: 248.6, 265.7) more visits per 100,000 people in 2011 in comparison to 2001. 27.1% of this difference could be explained by changes in the sociodemographic characteristics, where the following variables contributed the most: age, parents' country of birth, and father's educational attainment (Table 2, Study IV).

In 2011 compared to 2001, there were approximately 68 (95% CI: 62.0, 73.0) and 69 (95% CI: 62.2, 73.7) more hip OA surgeries and non-surgery visits per 100,000 people. Around 70.7% and 62.9% of the difference in hip OA surgery and non-surgery visits, respectively, were attributable to changes in the sociodemographic characteristics of the populations, while the remaining percentages were attributed to differences in the sociodemographic characteristics' coefficients and unmeasured factors. Age, parents' country of birth and father's educational attainment were the main determinants of the unexplained part for hip OA surgery and non-surgery OA visits. Of the previous mentioned variables, the latter contributed to a decrease in prevalence (Table 2, Study IV). Regarding the unexplained parts for the hip outcomes, following variables contributed considerably: age, educational attainment and country of birth, where the latter contributed to a decrease in prevalence. For the unexplained parts, unmeasured factors also had a major impact on how these outcomes changed over time.

Changes in educational inequalities

For both knee and hip OA surgery and non-surgery visits, the relative concentration indices were negative for all study years (values ranged from -0.28 in year 2001 to -0.11 in year 2011), showing that these outcomes were more concentrated among people with lower educational attainment (Figure 2, Study IV). In 2011 compared to 2001, the concentration indices for all outcomes were lower. Higher inequality was observed for OA surgery than for non-surgery visits for both knee and hip OA, with the difference being larger for the former than the latter (Figure 2, Study IV).

Table 3 in Study IV presents the sociodemographic factors' contributions to the changes in relative inequality between 2001 and 2011. The contributions of changes in the population characteristics (explained part) ranged from 15% (knee OA surgery) to 42% (hip OA non-surgery visits). Relative inequalities for all outcomes decreased when population age, civil status, and the proportion of people with a foreign background changed, while change in father’s educational attainment contributed to increase in relative inequalities (Table 3 Study IV). Unmeasured factors contributed substantially to a decrease in relative inequalities, while changes in the coefficients of sociodemographic parameters contributed primarily to an increase in relative inequalities. Age followed by mother's educational attainment, were the factors that contributed most to changes in relative inequalities over time among the sociodemographic characteristics.

The absolute educational inequalities in knee OA surgery and non-surgery visits increased from -33 (95% CI: -35, -31) and -53 (95% CI: -56, -50) per 100,000 people in 2001, respectively, to -44 (95% CI: -42, -46) and -67 (95% CI: -70, -63) in 2011. The absolute educational inequalities in the hip OA outcomes remained unchanged over time (Figure 3, Study IV).

Discussion

In this thesis, socioeconomic inequalities in fracture-related mortality and OA-related outcomes have been investigated. The studies included have, in general, shown socioeconomic inequalities in the studied outcomes in favour of people with high versus low educational attainment. In addition, study III, which had a twin study design, casted some doubts on the causal relationship between education and health inequalities. In the sections below methodological considerations, interpretation and possible implications of the results, as well as the magnitude of observed inequalities will be discussed.

Methodological considerations

This thesis is based on observational studies, and it is important to reflect on internal and external validity when interpreting the results. Internal validity is defined as the extent to which the presented results represent the true value being studied and this validity is affected by the methods used when collecting, analysing and interpreting the data. External validity, on the other hand, refers to the generalizability of the study (126)

Internal validity

Educational attainment as an indicator of SES

Educational attainment was an indicator for SES in all studies. As stated in the introduction, we chose educational attainment as an indicator of SES since the variable is widely accepted as an indicator of SES in health inequality research (6). However, there are some aspects that need to be taken into consideration when using the variable (6).

Firstly, as stated in the introduction, there might exist a reverse causality between educational attainment and health and/or there might exist factors that influence both health and SES (i.e. *the health selection hypothesis* and *the indirect selection hypothesis*). For instance, it has been reported that prematurity/low-birth weight is associated with lower educational qualifications in adulthood (127) as well as hip, but not knee, arthroplasty due to OA (128). Thus, possible health-benefits from education might be due to education per se or/and a difference in background health between different educational groups. We tried to take this into consideration in study III when adjusting for early-life physical fitness and BMI when examining the association between educational attainment and OA surgery.

All educational years are not created equal (129). When education is used as a continuous variable one assumes that every year of education contributes similarly to an individual's attained SES. This is problematic, since then it is assumed that a year of education at different ages/countries/educational institutions and eras are comparable, which they probably are not (6, 129). In study III and IV educational attainment was used as a continuous variable, however, in study III we did also present results when educational attainment was treated as a categorical variable.

Moreover, when using educational attainment as years of education or levels of attainment, the variable does not provide any information regarding the quality of the education or school (6). Furthermore, measure of formal education does not take informal education into consideration, which also may be of importance in a broader perspective (6).

Another important consideration when using educational attainment as an indicator of SES is that individual life chances and social opportunities are captured by educational attainment (130). Thus, educational attainment does not only reflect schooling. For instance, it has been reported that parents' educational attainment and choices are associated with their child's educational attainment (131, 132). In addition, it has been reported that parental circumstances affect child health (133). Based on this, it is possible that there exists parental confounding when studying educational health inequalities. However, in study III we tried to eliminate that possible confounder by using twin study design.

As stated in the introduction, the Swedish educational system has changed over the years. Because of this, one can hypothesize that the meaning of educational levels differs between birth cohorts. We tried to take this into consideration by adjusting for birth cohort in study III. Additionally, in study I and II three and two age groups were used, respectively.

Sex differences in educational attainment may be another important factor when studying educational inequalities in health (6). As stated in the introduction, in Sweden it is primarily among females the level of education has increased during the past decades (13) and this phenomenon has also been observed in many other high-income countries (134). Moreover, it has been suggested, by the so-called *resource substitution theory*[1], that females' health may be impacted by educational level more than men's health (135). Thus, it may be important to take sex into consideration when studying heath inequalities. In study I-III we took sex into

[1] According to the *resource substitution theory*, education increases well-being more for females since their socioeconomic disadvantage causes them to rely more on it to obtain well-being.

consideration by treating sex as a confounder. Moreover, we also conducted stratified analyses by sex in study I and II.

Validity of data used

The registers used to retrieve the data are considered to be reliable with a high coverage (90-92), however one cannot exclude that there might exist measurement errors in the variables used. There is a possibility for measurement errors in the education variable since self-reported data is being used in some cases. For instance, self-reported data on highest educational attainment is obtained from foreign-born people moving to Sweden (136).

What concerns assessment of mortality and underlying/contributing causes of death, the mortality data is based on information retrieved from death certificates, which in turn are coded by the responsible physicians and thus may be prone to bias. This might also apply to diagnosis codes in the SHR and the National Patient Register. Although the Cause of Death Register is considered to be a high quality register (90), problem with inaccurate mortality data in the register has been reported (137). Additionally, our findings may be biased if there are educational differences in the reporting of death causes and diagnoses (e.g., differences in OA diagnosis based on the patient's level of education due to health care avoidance in low educated or cognitive bias in physicians). What concerns study I, a study performed in the late 80s in the United Kingdom reported that fractures often are underreported on death certificates (138), and if this finding also applies to our data there might be a misrepresentation in the data.

As with the other registers used, the reliability of the National Patient Register is considered to be good and reflect the data available in the regional patient administrative systems (91). However, problems with data reporting to the register, mainly by private healthcare providers, have been reported (91).

Missing data

What concerns missing data, in study I, a relatively large proportion of fracture-related deaths (n = 987) occurred in subjects who were left out of the analysis because information about their educational attainment was absent. In comparison to the study population, the excluded group had a higher percentage of non-Nordic born individuals, which may have limited the generalizability of the results. In study II, 4,195 and 2,671 people were excluded from the OA-cohort and reference-cohort respectively. The percentage of people that were non-native (i.e. born abroad, or born in Sweden with both parents born abroad) were higher in the excluded group, which might also have affected the results.

Confounding

Study I-III are prone to unmeasured confounding. What concerns study I, there might exist other potential confounders that we have not adjusted for (such as parental characteristics and early-life environment etc.). Additionally, in study I, we considered non-hip fractures as one group, even though different fractures exhibit different characteristics concerning mortality and prevalence in age groups etc. This approach is a limitation since the studied association may be confounded by different confounders depending on fracture site. Regarding study II, as for study I, there might exist other potential confounders that we have not adjusted for (such as parental characteristics and early-life environment etc.). In study III we took parental characteristics and early-life environment into consideration when using twin data. However, we did not adjust for typical individual confounders like knee injuries etc., which is a limitation of the study.

Methodology

In study II, all-cause and cause-specific mortality was investigated by using the single-cause of death method. Since deaths most likely are caused by more than one disease (85), especially among the elderly, it is possible that useful information is lost when only taking the UCD into consideration. This is a limitation of the study. Initially, we tried to estimate RII by the so-called multiple causes of death approach using methodology developed by Moreno-Betancur et al. (139). However, the method was not feasible considering the large data set.

External validity

Study I and II were based on data concerning the region of Skåne. Since the investigated region's population has several traits in common with Sweden overall, including age, sex, migration patterns, employment, and the distribution of residents between urban and rural areas (140), it is likely that the findings of study I and II may be applied to the entire nation.

In study III, twin data from the STR was used and since twins are not a random sample of population one could speculate whether the findings are generalizable to the whole population of Sweden. In addition, it is voluntarily to participate in the STR which in turn introduces recruitment bias. If the included twins systematically differ (regarding relevant factors) from twins who reject to be a part of the STR then the study findings are biased and not generalizable. Furthermore, even though the methodology with co-twin control design has major strengths, there might be a problem regarding selection. Discordant twins are of interest when conducting a co-twin control study and one could hypothesize that exposure discordant twins may be a selected group, and not a representative sample for the general population.

Are the findings of the thesis applicable to other countries? In Sweden, the majority of healthcare expenditures are covered by the government, thus the system facilitates equal access to healthcare services. It may be difficult to apply the findings to other countries than Sweden due to that educational- and health care systems differs between countries. However, the results may be generalizable to populations living with similar educational- and healthcare systems as the one in Sweden.

Comparison to previous studies & interpretation and implications of findings

Educational inequalities in fracture-related mortality

Generally, fracture-related mortality was greater in low vs high educated people. The relative educational inequality was more pronounced in younger people, while the absolute educational inequality rose with age. Furthermore, there were educational inequalities in non-hip fracture-related mortality among people aged 30-69 years but not older.

No previous study had assessed the association between educational attainment and fracture-related mortality in the general population. However, the overall findings of this study are in line with research that have found an inverse association between educational attainment and post-hip-fracture mortality (48, 49), but in contrast with research that has found no association between education and post-hip fracture mortality (51). The study's results are also consistent with other studies that have used other indicators of SES (individual- or area-level based) than education and found an inverse association between SES and post-hip-fracture mortality (45, 141-143).

The findings are probably a result of many factors combined. The incidence of fractures might differ between educational groups. If the fracture incidence is higher among people with lower educational attainment, this group may have an increased risk of dying from fracture. For instance, people with high educational attainment are less likely to smoke and be physically inactive (20), which are factors associated with a higher risk of fracture (144, 145). It has also been reported that people with low educational attainment also have a higher risk of falls, assaults and traffic accidents (146), which can lead to fracture-related injuries. However, the evidence on the association between educational level and hip fracture incidence is inconsistent (41-44, 50). Besides possible educational differences in fracture incidence, there might exist educational differences in consequences after fracture due to, for instance, differences in background health and post-fracture care. People with lower educational attainment, generally, have poorer health status compared to people with high educational attainment (20) and the presence of comorbidities is a risk factor for post-hip fracture mortality (147, 148). Previous research has reported disparities in post-fracture care, where people with low SES receive a lower volume of care and longer time to surgery (45-47). Whether these kinds of disparities also exist in the region of Skåne is unknown.

The observed association between educational attainment and fracture-related mortality needs to be examined in more depth in order to be able to reduce the seen inequalities. However, the overall findings of the study suggest that one should target fracture prevention and treatment of people with low educational attainment.

Educational inequalities in all-cause and cause-specific mortality in OA patients

Higher all-cause and cause-specific mortality were seen in people with low education compared to those with high education, and this was seen among OA patients as well as references free of OA. The contribution of cardiovascular mortality to the absolute inequalities was greater in the OA cohort in comparison to the reference cohort. This finding reflects the greater burden of cardiovascular diseases in the OA cohort, especially in people with low educational attainment.

The relative inequalities in mortality were similar between the OA- and reference cohort, while the absolute inequalities were greater in the reference cohort. The latter finding may be due to a greater overall mortality in the reference cohort (23.8%) in comparison to the OA cohort (19.8%). This result is in line with some previous research that have reported lower mortality in OA patients in comparison to the general population (70, 71). The lower mortality has been suggested to be due to that OA patients that seek care for their joint pain may differ from OA patients that do not seek care regarding, for example, their general health (70, 71). Another theory is that OA patients who seek treatment receive treatment for both their OA and underlying health conditions (70, 71), which promotes their overall health. Since the educational disparities were present in both the OA- and reference cohort, the findings imply that the disparities present in the OA cohort reflect the disparities present in the general population. Consequently, health inequalities should primarily be addressed in the general population in order to even out observed inequalities among people with and without OA.

As described in the introduction of this thesis, socioeconomic health inequalities most likely arise due to many factors combined and the findings of this study are probably no exception to this. Possible theories and explanations include *the health selection hypothesis*, *the indirect selection hypothesis*, explanations that points to differences in *material* and *psychosocial* factors, *behavioural* differences and differences in *biomedical* factors (3).

The finding of greater contribution of cardiovascular mortality to the absolute inequalities in the OA cohort is consistent with previous research that have reported an association between increased cardiovascular mortality and OA (64, 66, 68, 72). It is possible to take preventative action in this specific group of patients by drawing attention to the observed inequality. For instance, one could try to reduce cardiovascular mortality in OA patients by implementing this finding in standardised OA management programs such as BOA through screening and initiation of treatment of cardiovascular risk factors.

Cancer-related mortality contributed more to the absolute inequality in the reference cohort in comparison with the OA cohort. There were minor differences between the cohorts regarding the distribution of cancer types causing deaths and this is one possible explanation for the finding, since there has been reported variations in the associations between different cancer types and SES (149). Another possibility is that the estimates in the reference cohort reflect the ongoing shift in leading cause of death from cardiovascular- to cancer-related deaths, which has been observed in high-income countries like Sweden (150). This shift has been suggested to be due to better treatment and prevention of cardiovascular diseases in high income countries and thus a reduction in cardiovascular mortality (150). If this is the cause for the higher contribution of cancer-related mortality in the reference cohort, it also highlights the importance of treatment of cardiovascular diseases in OA patients.

Association between educational attainment and knee and hip OA surgery

There was no conclusive association between educational attainment and knee OA surgery when taking genetics and early-life environment into account. On the other hand, the findings of the study suggest that the inverse association between educational attainment and knee OA surgery often reported in observational studies may be due to confounding of shared familial factors. Regarding hip OA surgery, our findings suggest no conclusive association between educational attainment and the outcome. Furthermore, our findings suggest no substantial familial confounding on the association.

Higher educational attainment has, in previous research, been reported to have a protective effect on OA outcomes (73-80, 151) and results supporting this was also seen in the study's unmatched cohort analyses for knee OA surgery. This association was, however, weakened when examining the within-pair effect on knee OA surgery in MZ twins, indicating that the estimates from the unmatched cohort analyses are confounded by familial factors such as genetics and/or early-life environment. This finding highlights the importance of taking familial factors into consideration when studying the impact of education on OA, and this may apply to other diseases as well. The finding of a familial effect on the association between educational attainment and knee OA surgery is consistent with the so-called *life course theory* described in the introduction of this thesis. *The life course theory* acknowledges that health in adulthood is influenced by early-life health and conditions (3, 152). What concerns the study's finding regarding familial confounding, one might speculate that, for instance, parental characteristics such as parental education most likely influence their child's health and perhaps in more specific the risk of OA surgery. Since parents' educational attainment is associated with their child's educational attainment (131), it might be possible that parental education is a confounder of the familial effect found in the study. Moreover, obesity is an important risk factor for knee OA (153-155), and it has been reported that parents' educational attainment is inversely associated with their child being overweight (156).

In the study we tried to take early-life health status in consideration by adjusting for BMI and physical fitness. The estimates from these analyses had very broad CIs, making it difficult to draw any firm conclusions. However, the estimates remained similar after adjusting for BMI and physical fitness, suggesting that these factors had little impact on the estimates.

That a family effect of educational attainment on knee OA surgery, and not hip OA surgery, was found in the study might reflect the fact that environmental factors seem to have a greater impact on the progression of knee OA in comparison to hip OA (59, 60, 157). As an example, it is known that genetics contribute more to hip than knee OA (58-60).

Since our results suggest no association between educational attainment and knee and hip OA surgery when using co-twin control design, interventions on education are unlikely to change the rates of OA surgery. Thus, OA prevention attempts should focus on other modifiable factors.

Changes in knee and hip OA surgery and non-surgery specialist care visits

The prevalence of all outcomes increased over time and this finding is consistent with previous research that have projected an increasing burden of OA (54, 158, 159). Changes in the strengths of the associations between sociodemographic characteristics contributed in large to the increased prevalence in knee OA outcomes. In contrast, the increased prevalence in hip OA outcomes were in large attributed to changes in the characteristics of the populations.

For all outcomes, age contributed the most to the unexplained part of the decomposition analysis, and our results suggest a weaker positive association between age and the studied outcomes in 2011 than in 2001. This finding is in line with previous research that have reported an increase in knee OA surgery in younger patients (<55 years) in Sweden from the late 90s to the time near 2010, and thus depicted that OA surgery is not limited to the older population (160).

The increase in prevalence of the hip OA outcomes, were in large attributed to an older population and higher proportion of Sweden-born parents in 2011 in comparison to 2001. Since age is an important risk factor for OA (55), the result concerning age is not surprising. However, it is unknown why the increase in prevalence is related to higher proportion of Sweden-born parents, but one could speculate that the finding reflects ethnical differences in hip OA outcomes, which previous research has suggested (161).

All outcomes were more concentrated among people with lower education in comparison with higher education. Thus, the higher burden of non-surgery specialist visits among people with lower education was also met with higher prevalence of OA surgery. The relative inequalities decreased during the study period for all outcomes. However, the absolute inequalities in knee OA outcomes increased, while the absolute inequalities in hip OA outcomes remained stable. This finding might suggest that the access to specialist care among people with lower education decreased during the studied time period. It is unknown if this potential decrease in access to specialist care is medically motivated, for example, as a result of improved management of OA at primary care in this group.

The finding of higher concentration of all outcomes in people with lower education is consistent with previous research that have found an inverse association between educational attainment and rate of knee OA surgery (80), and prevalence/symptoms of OA (73-79, 151). The result is most likely due to many factors combined. For instance, people with lower education may more often have physically demanding occupation, which has been suggested as a risk factor for knee and hip OA (162-164). The severity of OA might also vary between educational groups (77-79), which may affect the health care seeking behaviour. Moreover, given/accepted treatment might also differ between educational groups. For instance, it has been reported that people who participate in BOA, generally, have higher educational attainment (165). Additionally, it should be highlighted that the inequalities seen might be due to selection (see *the health selection hypothesis, the indirect selection hypothesis* described in introduction).

When decomposing the changes in educational inequalities a substantial part of the observed decrease between 2001 and 2011 were due to unmeasured factors. This finding suggests that there exist essential factors that we have not taken into consideration in our analyses.

The magnitude of observed inequalities

In study I, II and IV relative as well as absolute inequalities were examined, while only the former were examined in study III.

When reflecting on the importance of the findings of study I, the following questions are of interest: how large is the burden of fracture-related mortality? And, how do you interpret the magnitude of the found inequality? What concerns the burden of fracture-related mortality, 2.9% and 1.8% of all deaths in the study population during 1998-2013 were associated with non-hip fracture and hip fracture, respectively. Thus, fracture-mortality is not a great contributor to mortality compared to, for instance, cardiovascular mortality, which is the leading cause of death. As an example, cardiovascular mortality was the underlying cause of death in around 41% of all deaths in the Skåne region between 1998-2014 among people aged ≥30 years (166). However, as previously stated, fractures may be underreported on death certificates. Regarding the magnitude of inequality, no previous study has to our knowledge examined the association between SES and fractures as a cause of death, making it difficult to draw any conclusions about whether the inequalities seen are considered large or not in the context of fracture mortality. Study II, which examined educational inequalities in all-cause and cause-specific mortality, investigated the same geographical area during the same time period as study I and can be used to put the results of study I into perspective. However, when comparing the results, it is important to be aware that the reference cohort of study II was matched on age and sex against the OA cohort, making it a non-representative sample of the general population (for instance, the sample contained a higher proportion of females). In addition, the confounder considering country of birth was defined differently in the two studies. The SII (per 100,000 person-years) and RII in all-cause mortality were 543 (95% CI: 433, 653) and 1.34 (95% CI: 1.27, 1.41), respectively, among people aged ≥75 years in the reference cohort. In comparison, the SII (per 100,000 person-years) and RII in hip-fracture mortality, in study I was 110.0 (95% CI: 25.5, 194.5) and 1.3 (95% CI: 1.1, 1.6), respectively, among people aged ≥85 years.

Since SII and RII are well-established measures of inequality (116), there are numerous studies that have examined all-cause and cause-specific mortality using these indices (167-170). However, what concerns the magnitude of the inequalities observed in study II, it is difficult to compare the results with non-Swedish studies considering different countries have different educational- and heath care systems. The same reasoning, but concerning the concentration index, applies to the findings of study IV.

Conclusions

In this thesis I have studied socioeconomic inequalities in fracture-related mortality and OA-related outcomes via observational studies using individual-level register data analysed by different epidemiological methods. The overall conclusion of the thesis is that there exist socioeconomic inequalities in fracture-related mortality and OA-related outcomes in favour of people with higher SES. In addition, the studies have led to the following conclusions in specific:

- Findings suggest an inverse association between level of education and fracture-related mortality, which in turn suggests that preventative and therapeutic interventions for fractures should pay special attention to people with low educational attainment.

- People with lower education, with or without OA, have higher all-cause and cause-specific mortality compared to people with higher educational attainment. The educational inequalities in mortality in OA patients reflect the health inequalities in the population at large. Therefore, in order to eliminate the observed differences between people from various educational backgrounds, both with and without OA, these inequalities should first be addressed in the general population.

- Results suggest that OA patients, especially with lower education, have a greater burden of cardiovascular diseases. This implies that it is important to focus on prevention and treatment of cardiovascular diseases in OA patients.

- When adjusting for genetics and early-life environment, there seems to be no association between educational attainment and knee and hip OA surgery. However, there seems to be a confounding familial effect on the association between educational attainment and knee OA surgery but not hip OA surgery. Thus, the results suggest that the often reported association between education and knee OA surgery is due to familial confounding and that interventions on education are unlikely to change the rates of OA surgery. Consequently, OA prevention attempts should focus on other modifiable factors.

- In Sweden, the prevalence of knee and hip OA surgery and non-surgery specialist care visits increased from 2001 to 2011. Changes in the strength of the association between sociodemographic factors and OA outcomes contributed the most to the increase in prevalence of knee OA outcomes. For hip OA outcomes, the increase was, on the other hand, primarily due to changes in age and parents' country of birth over time. What concerns inequalities, all outcomes were more concentrated among people with lower education. Furthermore, absolute educational inequalities were either decreasing or steady over time, while there was a declining tendency in relative inequalities for all outcomes.

Future perspectives

Finally, this research has given rise to many questions in need of further investigation. What concerns fracture-related mortality, future studies should examine the found inverse association between educational attainment and fracture-related mortality in more depth. As a suggestion, the fracture incidence by level of education in the Skåne region during the studied time period should be examined in addition to time to surgery for hip fracture patients.

Regarding socioeconomic inequalities in all-cause and cause-specific mortality among OA patients, one should preferably investigate the examined association using a multiple cause of death approach. This would possibly capture a more accurate picture of mortality and its associations.

In study III we did not account for typical individual-level confounders such as previous injuries etc., which most likely are important when studying the association between educational attainment and OA surgery. Thus, it would be interesting to take this in considerations into future studies.

Concerning the study of changes in knee and hip OA outcomes, future studies should include additional characteristics to the decomposition analyses (for instance physical activity level, body mass index, disease severity, and health status etc.). This is because only a small portion of the change in prevalence of knee OA outcomes and in educational inequalities of the outcomes could be explained by the characteristics included in the study. In addition, it would also be interesting to include data from the primary care, in order to give a more comprehensive view on the changes of OA over time in Sweden.

Populärvetenskaplig sammanfattning (Summary in Swedish)

Muskuloskeletala sjukdomar, dvs rörelseorganens sjukdomar, orsakar stort lidande för många människor i Sverige och globalt sett. Två viktiga muskuloskeletala sjukdomar är benbrott, även kallat frakturer, och artros. Frakturer är vanligt förekommande och bidrar med stora samhällskostnader förutom att orsaka personligt lidande och till och med, i vissa fall, död. Exempelvis avlider ca 30% av de individer som drabbats av höftfraktur inom ett år efter frakturtillfället. Artros är den vanligaste förekommande ledsjukdomen och kännetecknas av nedbrytning i ledbrosket och förändringar i ledrelaterade strukturer, vilket i sin tur leder till ledsvikt. Liksom för frakturer bidrar artros till stora samhällskostnader och lidande. Enligt hälso- och sjukvårdslagen (2017:30) är målet för hälso- och sjukvården en god hälsa och en vård på lika villkor för hela befolkningen. Emellertid finns det ett välkänt samband mellan socioekonomisk status (SES) och hälsa, där personer med lägre SES tenderar att, generellt sett, ha sämre hälsa och ökad dödlighet jämförelsevis med personer med högre SES. Detta fenomen är globalt och benämns som *den sociala gradienten i hälsa*. Den sociala gradienten i hälsa har observerats gällande dödlighet såväl som för ett brett spektrum av sjukdomar, inklusive muskuloskeletala sjukdomar. Emellertid är socioekonomiska ojämlikheter i muskuloskeletala sjukdomar inte ett välstuderat område.

Det övergripande målet med detta avhandlingsarbete var att undersöka sambandet mellan SES och utfall relaterade till frakturer och artros, i syfte att identifiera möjliga ojämlikheter i hälsa.

Avhandlingen består av fyra så kallade observationsstudier som i sin tur är baserade på registerdata på individnivå från personer bosatta i Skåneregionen (studie I och II) och hela Sverige (studie III och IV). För alla studier användes utbildningsnivå som en indikator för SES. Följande datakällor användes i avhandlingen: Statistiska centralbyrån (Registret över totalbefolkningen och Longitudinell integrationsdatabas för sjukförsäkrings- och arbetsmarknadsstudier), Socialstyrelsen (Dödsorsaksregistret och Patientregistret), Skånes Häsloregister, Svenska Tvillingregistret och Mönstringsregistret. Olika statistiska mått och metoder användes för att beskriva samband och analysera datan, däribland slope index of inequality (SII), relative index of inequality (RII), Weibull within-between shared frailty model, koncentrationsindex och Blinder-Oaxaca dekomponering.

I den första studien, som totalt inkluderade 999 148 individer, undersöktes utbildningsskillnader i frakturrelaterad dödlighet för icke-höftfrakturer respektive höftfrakturer. Studien var en så kallad öppen kohortstudie där personer i ådern 30-99 år bosatta i Skåne under 1998-2013 följdes fram till något av följande scenarier: död, deras 100-årsdag, flytt utanför Skåne eller slutet av 2014. Resultaten kunde visa att den frakturrelaterade dödligheten var högre hos lågutbildade jämfört med högutbildade. Resultatet i sig antyder att man framförallt bör fokusera på frakturförebyggande och behandlade insatser hos personer med låg utbildningsnivå. Emellertid bör det studerade sambandet studeras i mer detalj för att man på sikt ska kunna jämna ut den observerade ojämlikheten.

I den andra studien undersöktes och jämfördes utbildningsskillnader i dödlighet hos artrospatienter med utbildningsskillnader i dödlighet hos artrosfria personer. All typ av dödlighet samt dödlighet i de fem vanligaste förekommande dödsorsakerna undersöktes. Liksom studie I var detta en öppen kohortstudie och alla personer i åldern 45 år eller äldre med läkardiagnostiserad artros bosatta i Skåne mellan åren 1998 och 2013 följdes fram till något av följande scenarier: död, flytt utanför Skåne eller slutet av 2014. Totalt inkluderades 123 993 och 121 318 med respektive utan artros. Studien visade att personer med lägre utbildning, med eller utan artros, har högre dödlighet jämfört med personer med högre utbildning och att de observerade ojämlikheterna hos artrospatienter speglar ojämlikheterna i befolkningen i stort. Vidare antydde studiens resultat en högre börda av hjärt-kärlsjukdomar hos artrospatienter, jämfört med hos artrosfria personer, och att det således är viktigt att fokusera på prevention och behandling av hjärt-kärlsjukdom i denna grupp.

I den tredje studien undersöktes sambandet mellan utbildningsnivå och kirurgisk behandling av knä- respektive höftledsartros genom att analysera tvillingdata. Som föregående studier var även detta en öppen kohortstudie och alla tvillingar i det Svenska Tvillingregistret i åldern 35-64 år följdes från 1:a januari 1987 eller datumet de fyllde 35 år till något av följande scenarier: död, flytt utanför Sverige eller slutet av 2016. Totalt inkluderades 67 071 tvillingar (18 784 kompletta tvåäggstvillingspar och 8 657 kompletta enäggstvillingar). Sambandet mellan utbildningsnivå och kirurgi undersöktes i olika modeller där man bland annat tog hänsyn till faktorer som tvillingar i ett tvillingpar delar så som genetik (i varierande grad beroende på två- eller enäggstvillingar) samt tidig livsmiljö. Då man justerade för genetik och tidig livsmiljö kunde man ej påvisa något samband mellan utbildningsnivå och artroskirurgi varken vad gäller knä eller höftledsartros, och följaktligen bör artrosförebyggande arbete fokusera på andra modifierbara faktorer än utbildningsnivå. Vidare antydde studiens resultat att det finns en familjeeffekt på sambandet mellan utbildningsnivå och artroskirurgi rörande knäledsartros, dvs att familjefaktorer så som exempelvis föräldrars SES eller liknande påverkar sambandet.

I den fjärde, och sista, studien undersöktes förändringar av befintliga fall, så kallad prevalens, och utbildningsskillnader i artroskirurgi och icke-kirurgiska specialistbesök rörande knä- och höftledsartros i Sverige. Dessutom undersöktes i vilken utsträckning sociodemografiska faktorer kunde förklara förändringarna. Den undersökta tidsperioden var mellan åren 2001 och 2011 och alla individer i åldern 35 år och äldre bosatta i Sverige under perioden inkluderades. Prevalens och socioekonomisk skillnad i utfallen beräknades för varje år. Vad gäller undersökning av sociodemografiska faktorers betydelse, jämfördes endast år 2001 med 2011 och dessa två studiepopulationer bestod av 4 794 693 respektive 5 359 186 individer. Resultaten av studien visade att prevalensen för alla utfallen ökade från 2001 till 2011 och att förändringar i styrkan av sambandet mellan sociodemografiska faktorer och utfall bidrog mest till ökningen av prevalensen gällande knäledsartros. För höftledsartros berodde prevalensökningen istället på förändringar i studiepopulationens karakteristika i form av förändringar i ålder och föräldrars födelseland. Vad gäller utbildningsskillnader kunde studien visa att alla utfall var överrepresenterade hos personer med lägre utbildning under hela studieperioden. Vidare visade resultaten att de absoluta utbildningsskillnaderna ökade alternativt var stabila under tidens gång medan de relativa utbildningsskillnaderna minskade.

Avhandlingens övergripande slutsats är att det finns socioekonomiska ojämlikheter i frakturrelaterad dödlighet och artrosrelaterade utfall i förmån för personer med högre SES. Sambanden och underliggande mekanismer måste undersökas i mer detalj för att man ska kunna vidta åtgärder för att minska de observerade skillnaderna. Emellertid, kan man se denna forskning som ett första steg mot att minska ojämlikheter eftersom det är nödvändigt att först identifiera och kartlägga skillnader.

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